PSJ2 Exh 112

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Recurrence:	(none)
Meeting Status:	Not yet responded
Organizer:	Jordheim, Amy
Required Attendees:	Robinson, Dean; Castagno, Paula; Day, Matthew; Reedy, Katherine; Condrige, Jeffrey; Savitt, David; Fishbein, Sean

When: Tuesday, November 25, 2008 9:00 AM-9:30 AM (GMT-07:00) Mountain Time (US & Canada).
Where: teleconference

~~*~*~*~*~*~*~*~*

Our apology for scheduling this meeting mid-day. <<FENTORA Premodule FINAL.pdf>>

The objectives for this meeting are to review the current oncology training piece and to begin development of the January deliverable.

The notes from the last meeting are in process and we will get them out to you shortly. Please review the attached module (specific to the oncology sections) and come prepared to present what you like and where you feel they could be added upon. If you would like to put your ideas in a bulleted format (send to Amy), we will place your ideas in the slide deck we are creating for Tuesday's meeting. If you want to simply discuss your ideas, that is also fine.

Please also bring your ideas for the slide deck that Area Managers will use to share this idea with their teams in January.

We look forward to speaking with you next week.

Sean and Amy

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Pre-module

Introduction to Pain

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Introduction

In 1960, the first multidisciplinary pain clinic was established by John J. Bonica in Seattle, Washington. Bonica brought together clinical and basic researchers to improve the effectiveness of pain management. By the 1970s, he had developed the first formalized training program in pain management. In 1973, Bonica developed the International Symposium on Pain from which came the International Association for the Study of Pain, composed of physicians, nurses, dentists, physical and occupational therapists, psychologists, social workers, pharmacists, and basic scientists. His goal was to make pain management an integral part of health care and to increase research on pain. *[IASP, 1994, 2]*

In the 1980s, an increasing number of professional publications and reviews addressed multiple aspects of pain including patient factors, assessment, professional standards, and treatment options. Despite this professional attention, in 1999, the Joint Commission on Accreditation of Healthcare Organizations (The Joint Commission, or JCAHO), identified pain as a major yet largely avoidable health problem. Resulting Joint Commission initiatives include new standards for pain management that are necessary for healthcare organizations that the Joint Commission accredits.

Good pain control should be a high professional priority. Unrelieved pain causes unnecessary suffering. Since pain reduces activity, appetite, and sleep, it can further weaken already debilitated patients. The psychological impact of cancer pain can also be devastating. Patients with cancer often lose hope when significant pain emerges, and believe that pain signals the unstoppable progress of the disease.

This learning system will introduce you to several of the reasons pain is still undertreated. This model implies that the pain should be managed by a single "right" dose of an analgesic medication. However, this frequently simplifies the real nature of pain.

Many patients have exacerbations of pain that are caused by either predictable events such as increased activity or by unpredictable internal physiologic events. In 1990, Drs. Portenoy and Hagen described breakthrough pain as a transitory exacerbation or flare of moderate to severe pain in patients with otherwise stable persistent pain. Since then, breakthrough pain has become the focus of increasing attention and recognition.

This module of the learning system will provide you with the physiologic background that you will need to understand how pain signals are transmitted in the nervous system and how pain is inhibited by descending pathways that are influenced by opioid medications. It also provides you with information on the classification of pain, how it is medically evaluated, and pain syndromes associated with cancer.

Tips for Effective Study

This module is arranged for easy study. Note the following features as you study the module, and then review what you have learned.

1. The text is clearly divided into sections and subsections, with brief introductions that preview what you will be learning. Use the introductions to help orient yourself to the content ahead.

2. Glossary terms appear in **red** the first time they are used in the text.

3. The fast track also summarizes the main points of each paragraph. Use the fast track to go back later and review what you have read, as well as find information quickly later.

4. Summaries and review questions follow text sections. Use them to help confirm that you have mastered the section's major points.

5. The post-test is followed by an annotated answer page. Use the text references to review any material you missed.

6. The modules build sequentially. Complete your study of the preceding module(s) before going on to the next in the series.

7. Reinforcement text appears throughout the module to:

   - highlight tips and relevant information
   - summarize and question key learning points, and
   - link you to earlier module(s) or prepare you for new information in upcoming section(s) or module(s)

The identifiers below are examples of how important information is highlighted or reinforced for the reader.

Tip:
This kind of box tells you about related facts and materials that you may find useful while reading, or helps you relate this material to disease or product information.

Look For/Remember:
This kind of box lets you know that materials are covered in more depth in another section or module.

Learning Objectives

Learning objectives provide a guide for specific and measurable knowledge and understanding that you should have at the conclusion of training. After you finish this module, you will be able to meet the following objectives.

1. Distinguish acute from chronic pain.
2. Identify the features of somatic, visceral, and neuropathic pain.
3. Describe common causes of cancer pain.
4. Distinguish persistent pain from breakthrough pain, and identify subtypes of breakthrough pain.
5. Describe the role of A-delta and C fibers in the transmission of pain.
6. Identify major components of the physical examination of the pain patient.
7. Identify the impact of several psychosocial factors affecting pain reporting.

Recommended Preparation: Please take time to review the terms and definitions in this glossary. These terms appear in **red** at their first substantive occurrence in the text to remind you that they are defined in the glossary.

Glossary

Addiction: chronic disease that is characterized by one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving for a medicine.

Afferent [AF uhr uhnt]: describing sensory nerve pathways that carry impulses from sensory receptors to the CNS; the opposite of efferent.

Allodynia [AL oh DIN ee uh]: pain sensation elicited by a non-painful stimulus (eg, light touch); results from nerve inflammation at the site of injury.

Anaplastic [AN uh PLAS tik]: referring to the loss of cellular differentiation.

Around-the-clock (ATC) dosing: referring to medications that are given on a regularly scheduled basis to manage persistent pain.

Aspartate [as PAR tayt]: excitatory neurotransmitter in all regions of the central nervous system.

Autonomic nervous system: portion of the peripheral nervous system involved in regulating involuntary activity (eg, cardiac muscle, smooth muscle, and glands).

Benign: referring to a tumor that is not malignant; such tumors are usually surrounded by a fibrous capsule.

Bradykinin [BRAD ee KI nin]: substance produced by the body in a variety of inflammatory conditions, including injury.

Breakthrough pain: transitory exacerbation or flare of moderate to severe pain in patients with otherwise stable, persistent pain.

Central nervous system (CNS): portion of the nervous system composed of the brain and spinal cord.

Cerebral cortex: outer brain layer responsible for conscious perception, information processing, and thought.

Colicky: when referring to pain, an acute, intermittent abdominal pain.

Cranial nerves: group of 12 nerves that exit the brainstem and are involved in sensory and motor functions of the face, head, pharynx, larynx, and visceral organs.

Cutaneous: relating to the skin.

Differentiation: process of acquiring specialized form or function, as occurs in the development of cells and tissues.

Dorsal horn: dorsal (back) portion of the spinal cord gray matter containing neurons that process sensory information.

Dysesthesia [DYS es THEE zee uh]: any unpleasant abnormal sensation, including burning and tingling associated with neuropathic pain.

Efferent [EF uhr uhnt]: describing motor nerve pathways that carry impulses outward from the CNS to the body; the opposite of afferent.

End-of-dose failure pain: type of breakthrough pain occurring at the end of the regular dosing interval (eg, pain occurring 10–11 hours after giving a medication dosed every 12 hours). This pain is best managed by adjusting the dosage or timing of the around-the-clock medication.

Endorphins [en DOR finz]: analgesic neurochemicals produced within the CNS that act like "endogenous morphine." These are active at many brain and spinal cord locations, and play a part in pain perception, mood, and behavior.

Fibrosis [figh BROH sis]: formation of fibrous tissue, or scarring.

Glutamate: excitatory neurotransmitter in all regions of the central nervous system. In the spinal cord, glutamate is a pain transmitter between A-delta/C fibers and spinal neurons, which have glutamate-sensitive NMDA receptors.

Histamine: biologically active substance produced in many cells of the body and often released in allergic reactions; histamine causes vasodilation, increased permeability of blood vessels, and bronchial constriction.

Hyperalgesia [HIGH pur al JEE see uh]: change in pain sensation due to injury; in the area of an injury, normally mild painful stimuli are experienced as more painful.

Incident pain: type of breakthrough pain precipitated by an identified event (eg, walking, coughing).

Metastatic [MET uh STAT ik]: referring to cancerous cells that have spread from the point of origin to a different body site or organ.

Myelin [MIGH uh lin]: fatty substance that surrounds the axon and serves as an electric insulator.

Neoplasm: any new and abnormal growth; typically, an uncontrolled, progressive growth. It may be benign or malignant.

NMDA receptor: receptor in the central nervous system sensitive to the transmitter glutamate; in the spinal cord, NMDA receptors are involved in pain modulation and transmission between incoming A-delta/C fibers and spinal neurons.

Nociceptors [NOH sih SEP tuhrz]: receptors in tissue sensitive to noxious and irritating stimuli; stimulation produces impulses perceived as pain by the brain.

Norepinephrine [NOR ep in EF rin]: neurotransmitter released in both the peripheral nervous system and in some brain neural pathways.

Oncology: study of tumors.

Opioid receptor: site on a neuron that reacts selectively to natural opioids or opioid drugs.

Opportunistic infections: infections resulting from microorganisms that usually can only cause disease in persons with seriously compromised immune systems.

Paresthesia [PAHR uhs THEE zhuh]: abnormal sensation, such as burning, pricking, tickling, or tingling.

Parietal [puh RIGH eh tul]: referring to the lobes of the brain that lie under the crown of the skull.

Peripheral [pur IF er uhl] nervous system (PNS): all nerves and neurons lying outside of the brain and spinal cord.

Persistent pain: background pain that is present most of the day, every day; it is best managed by medications dosed on a regular schedule (around-the-clock).

Physical dependence: occurs when the body has gotten used to having the drug in its system. If the patient suddenly stops taking the drug, they feel sick (ie, withdrawal syndrome). If opioids are used for a long period of time, it is expected that the patient will become physically dependent on the medicine.

Plexus: network of peripheral nerves.

Prostaglandins [PRAHS tuh GLAN dinz]: class of biological substances that increase pain sensation in the peripheral tissues by sensitizing nociceptors to substances released during inflammation or injury.

Radicular [rah DIK yoo lahr]: referring to pain from disease or compression of the spinal nerve roots.

Rating scales: instruments used by the clinician to obtain measurable data about a patient's symptoms and/or functioning.

Sensitization: increased responsiveness of the nervous system or other bodily systems to a stimulus, which occurs as a consequence of the first exposure.

Serotonin [SAYR uh TOH nin]: potent vasoconstrictor and neurotransmitter.

Spontaneous/idiopathic pain: subset of breakthrough pain with no identified precipitating event and not related to the timing of the around-the-clock medication.

Substance P: small peptide in the nervous system; it is believed to be a transmitter in pain, touch, and temperature pathways.

Thalamus [THAL ah mus]: deep brain structure that relays sensory information entering the brain to the cerebral cortex.

Thrombosis [thrahm BOH sis]: development of a blood clot on the wall of a blood vessel.

Tolerance: occurs when the body gets used to the medicine and its effects. It may mean a stronger amount of medicine is needed to maintain pain relief. Tolerance can also occur when the body gets used to some of the medicine's side effects, such as nausea. This means that over time the patient will not feel these side effects or the side effects will be less bothersome to the patient. Tolerance is not addiction.

I. THE NERVOUS SYSTEM AND PAIN

The nervous system senses physical stimuli in the tissues, interprets the pattern and type of incoming information, and directs the muscles, endocrine glands, and other tissues to act in response. Both the central and peripheral nervous systems are involved in the complex events that lead to the perception of pain. The central nervous system is composed of the brain and spinal cord, while the other nerves make up the peripheral nervous system. The simplest pain sensation and response is the automatic, reflex withdrawal of the hand or other body part from a painful stimulus. However, most human pain perception is far more complex. There are both ascending or afferent pain pathways (nerve fibers carrying pain signals from the periphery to the spinal cord and brain) and descending or efferent pain pathways (nerve tracts from the brain to the spinal cord which carry, among others, signals that limit or "gate" pain transmission from the periphery).

A. The Neuron

The neuron is composed of three segments: dendrites (receive information), the cell body, and the axon (transmits information).

The cell that conveys information within the nervous system is known as a neuron. The neuron is composed of three major segments: dendrites that receive information, the cell body, and the axon, which transmits signals away from the cell body (see Figure 1). The cell body of a neuron is a ball-shaped structure. The axon, or nerve fiber, is an extension of the cell body. The length of a neuron ranges from less than 1 mm in length to several meters. Nerves are bundles of axons lying next to each other. *[Martini, 2006, 380–382; Sugerman, 2006, 412–413]*

Nerves are bundles of axons.

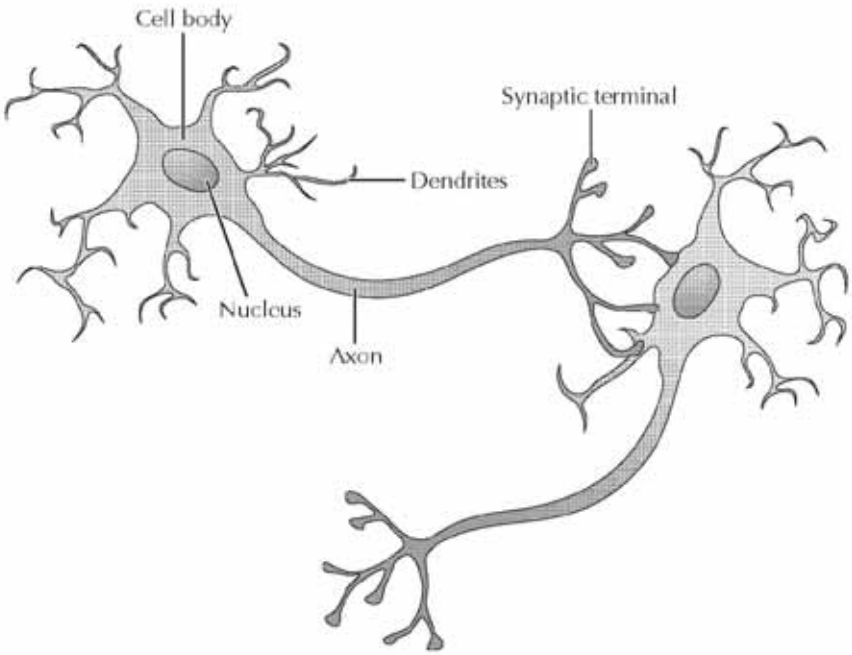


FIGURE 1

Anatomy of a neuron: dendrites receive information from other neurons, while axons transmit information to other neurons.

B. Peripheral Nervous System

The experience of pain is a function of the sensory nervous system. Sensory receptors of pain, called free nerve endings, are found in all tissues of the body. While large numbers of free nerve endings are found in skin, muscle joints, and walls of arteries, they also appear less densely in most of the internal organs. Receptors which respond to noxious (unpleasant, potentially harmful) stimuli are called **nociceptors**. Nociceptors transduce (convert) various stimuli into electrical activity for transmission to the central nervous system (CNS). *[Huether, 2006, 448–449]*

Pain receptors are free nerve endings.

Receptors responding to noxious stimuli are called nociceptors.

Nociceptors respond to three types of noxious or tissue-damaging stimuli: mechanical changes such as stretching or compression, thermal events (extreme cold or heat), and chemical stimuli related to tissue injury. Substances such as **histamine**, **bradykinin**, and **prostaglandins** are released in the tissues around nociceptors. It is

Biochemical substances (histamine, bradykinin, and prostaglandins) interact with free nerve endings in initiating and perpetuating pain sensations.

thought that these biochemical substances interact with free nerve endings and play a variety of roles in initiating and perpetuating pain sensations. For example, bradykinin activates pain fibers and produces pain by local application. The prostaglandins facilitate the pain response but do not evoke pain by themselves. Histamine release occurs under a variety of conditions, including injury and allergic reactions; histamine release has effects such as vasodilation, increased blood vessel permeability, and bronchial constriction. Potassium, acetylcholine, and hydrogen ions may also stimulate nociceptors. *[Carver, 2005, 2; Yaksh, 2004, 16, Guyton, 2006, 202, 480, 599; Huether, 2006, 448, 453]*

Afferent fibers transmit information from the periphery to the CNS.

Afferent fibers transmit information from the periphery to the CNS (see Figure 2). These fibers are classified as A, B, and C based on their size (diameter) and conduction velocity. A and C fibers are at opposite ends of the spectrum: A fibers are larger/faster conducting, while C fibers are thinner/slower conducting. In addition to sensations such as touch and pain, afferent nerve endings may transmit autonomic nerve information regarding the status of visceral organs (eg, heart, bladder). All of this information is transmitted to the CNS for possible action. *[Martini, 2006, 380; Guyton, 2006, 600; Fausett, 2004, 28–29]*

Efferent fibers conduct information from the CNS to the body.

Efferent fibers conduct information from the CNS to the body to perform activities such as muscle movement (see Figure 2). Other actions initiated by efferent nerves include organ responses, changes in the size of blood vessels, body temperature, and sweating. *[Martini, 2006, 380; Guyton, 2006, 748]*

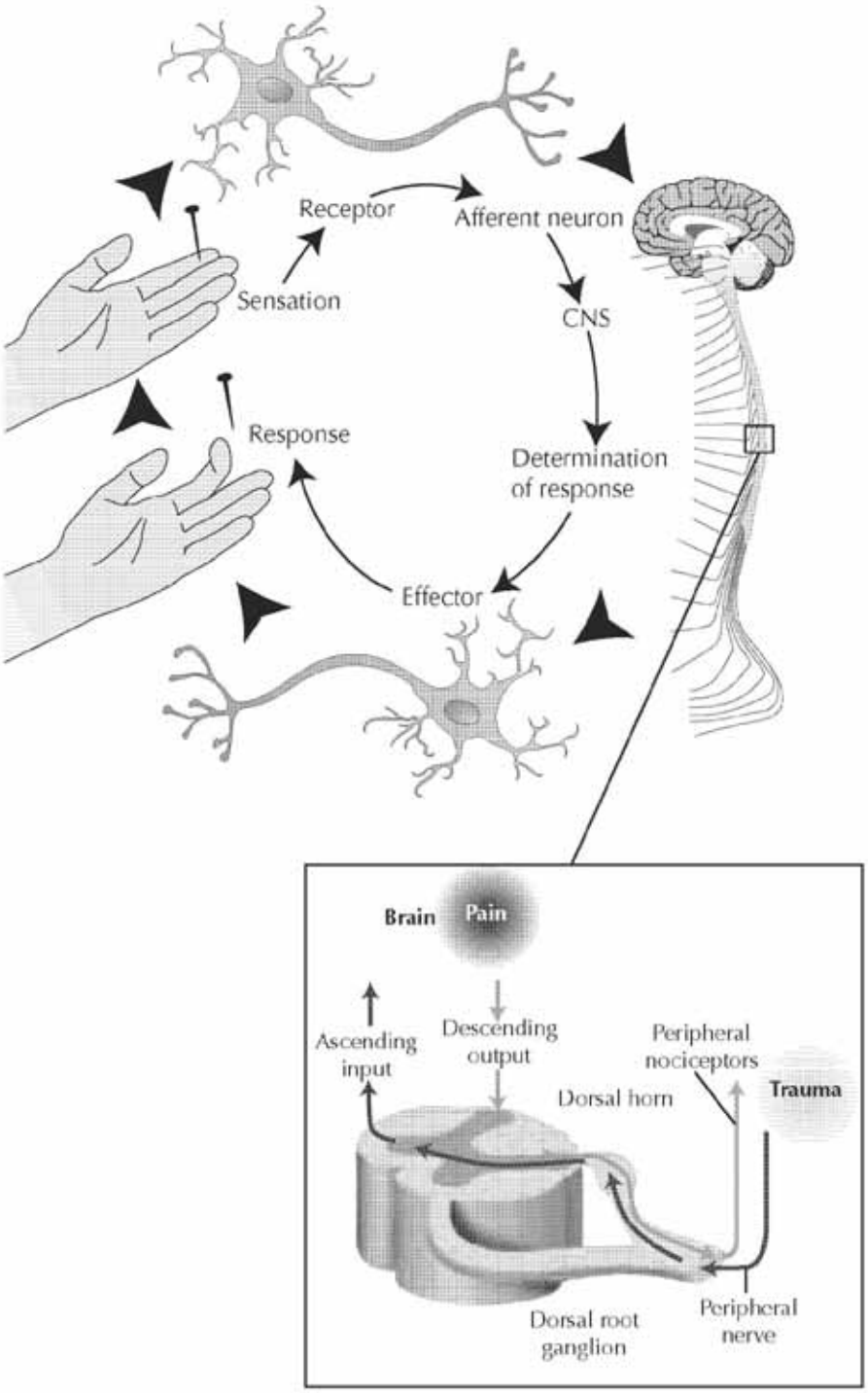


FIGURE 2

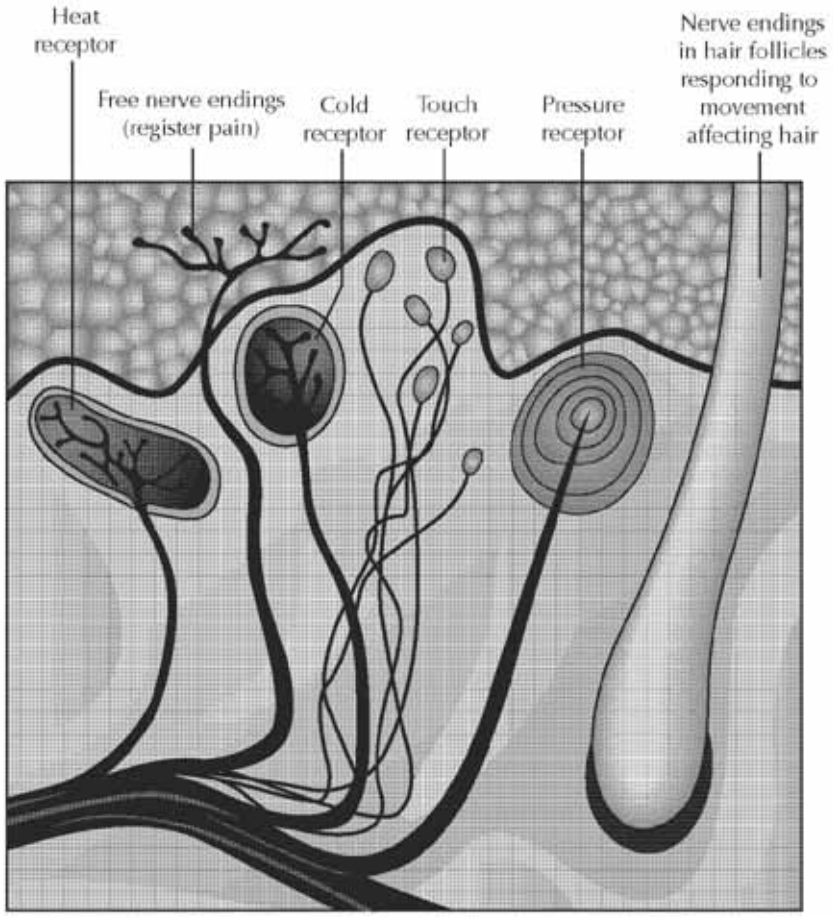
Afferent and efferent neurons: afferent neurons carry information to the CNS; efferent neurons carry responses from the CNS.

Pain is carried by A-delta fibers and by C fibers.

As shown in Figure 3, the receptors for temperature, touch, and pressure are specialized nerve endings, while pain endings are naked or free nerve endings. Pain is carried by a subtype of A fiber, the A-delta (Aδ), and by C fibers. *[Guyton, 2006, 573, 598, 600]*

FIGURE 3

Specialized receptors and free nerve endings: free nerve endings are receptors of pain, while specialized receptors respond to other stimuli.



A-delta fibers are covered by myelin, and conduct impulses more quickly than the uncovered C fibers.

Some A-delta fibers respond to intense or noxious mechanical stimulation, while other A-delta fibers respond to noxious heat or cold stimuli. The C fiber receptors respond to a wide variety of noxious stimuli, including intense mechanical events, heat, and cold. A-delta fibers are covered by **myelin**, and conduct impulses more quickly than the uncovered C fibers. Subjectively, this difference in transmission can be experienced. Brief noxious stimuli to human skin produce two distinct sensations: an early, sharp pain

mediated by the myelinated fibers and a later, duller pain produced by the action of the unmyelinated C fibers. Repeated stimulation of C fibers increases the sensitivity of these fibers, a process known as **sensitization**. *[Fausett, 2004, 28–29; Carver, 2005, 2, 4]*

C. Central Nervous System

The central nervous system (CNS), shown in Figure 4, is composed of the brain and the spinal cord. The brain receives and processes sensory input from the body via the **cranial nerves** and spinal cord. In general, the **cerebral cortex** of the brain processes sensory information received from the environment and body, is

The cerebral cortex processes information from the environment and the body.

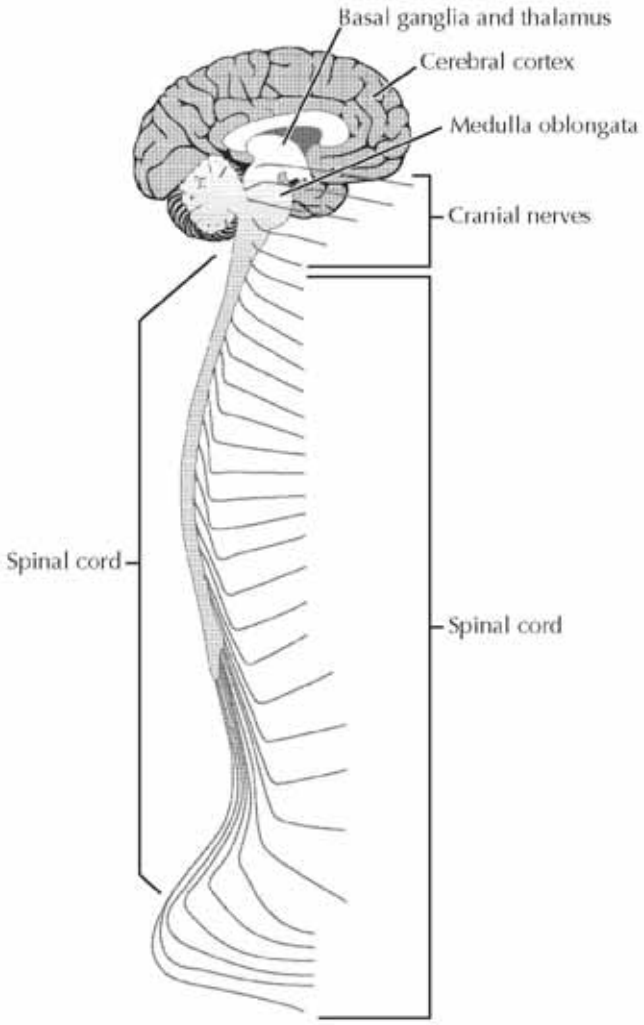


FIGURE 4

Components of the central nervous system: the spinal cord is capable of generating reflex actions, while perceptions, emotions, and cognitive functions arise from brain processes.

responsible for most of our thought processes, and is important for most of the storage of memory. Deeper areas of the brain, such as the basal ganglia, are responsible for more basic processes such as emotions, pain, and pleasure. The **thalamus** is a relay center for sensory information located in the central area of the brain. The medulla oblongata (situated at the base of the brain) controls body functions such as breathing, vomiting, heart rate, and blood pressure. *[Martini, 2006, 380; Guyton, 2006, 557–558; Sugerman, 2006, 419; Woodruff, 2004, 58]*

The thalamus is a relay center for sensory information.

The spinal cord passes information back and forth between the brain and peripheral nervous system, and initiates simple reflex actions, such as hand withdrawal from a painful stimulus. *[Guyton, 2006, 558]*

The spinal cord relays information between the brain and peripheral nervous system.

D. Neurotransmitters and the Role of Opioids in Pain Pathways

Afferent fibers collect into large nerve fibers before they enter the spinal cord at the **dorsal horn**. Once in the spinal cord, these fibers end on neurons in the gray matter of the spinal cord (substantia gelatinosa). As shown in Figure 2 on page 15, these fibers convey sensory information (including pain) to the spinal neurons, whose axons travel toward the brain in tracts (pathways), thereby transmitting the information to the brainstem and then to the cerebral cortex. The connection between the A-delta and C fibers and the spinal neuron is made by chemical transmitters. These chemical substances released from the A-delta and C fibers influence the electrical activity of the spinal neuron and the pain signal it transmits to the brain. *[Guyton, 2006, 601; Huether, 2006, 450, 454; Fausett, 2004, 30; Carver, 2005, 2; Woodruff, 2004, 57]*

Peripheral fibers end on neurons in the substantia gelatinosa.

From the substantia gelatinosa, axons travel toward the brain in tracts.

Several different neurotransmitters are released by the A-delta and C fibers. In the spinal cord, the primary excitatory transmitter substances are **glutamate** and **aspartate**.

The primary excitatory transmitter substances in the spinal cord are glutamate and aspartate.

Glutamate is believed to be secreted by both A-delta and C fibers and acts instantaneously on a number of different types of receptors on dorsal horn neurons, including the AMPA receptor, which may mediate fast pain, and **NMDA receptor**, which mediates **persistent pain**. *[Huether, 2004, 454; Guyton, 2006, 601; Fausett, 2004, 30; Cervero, 2003, 35, 39]*

Glutamate appears to play a role in fast pain and persistent pain.

Another neurotransmitter, **substance P** appears to be secreted by C fibers to act on the NK-1 receptor, playing a role in slow-chronic pain. *[Guyton, 2006, 601; Cervero, 2003, 39]*

Substance P appears to play a role in slow-chronic pain.

Binding of neurotransmitters to receptors results in electrical changes on the membrane of the spinal neuron. Once a threshold has been reached, the electrical changes travel up the axon to the brain. The pain impulse travels up to and through the medulla, to the thalamus, and then to the **parietal** area of the cerebral cortex. Figure 5 on the next page shows the connection between the A-delta and C fibers with the spinal neuron and the resulting pain transmission toward the brain. *[Sugerman, 2004, 415; Huether, 2004, 450–451, 453]*

The pain impulse travels up to and through the medulla, then to the thalamus, and then to the cerebral cortex.

In 1965, Melzack and Wall proposed a theory that explained the relationship between pain, tactile input, and emotion. They held that pain perception is influenced by tactile and emotional factors. According to this gate control theory, pain signal gating (blocking) occurs within the spinal cord. *[Huether, 2006, 448, 450, 452]*

Pain signal gating (blocking) occurs within the spinal cord.

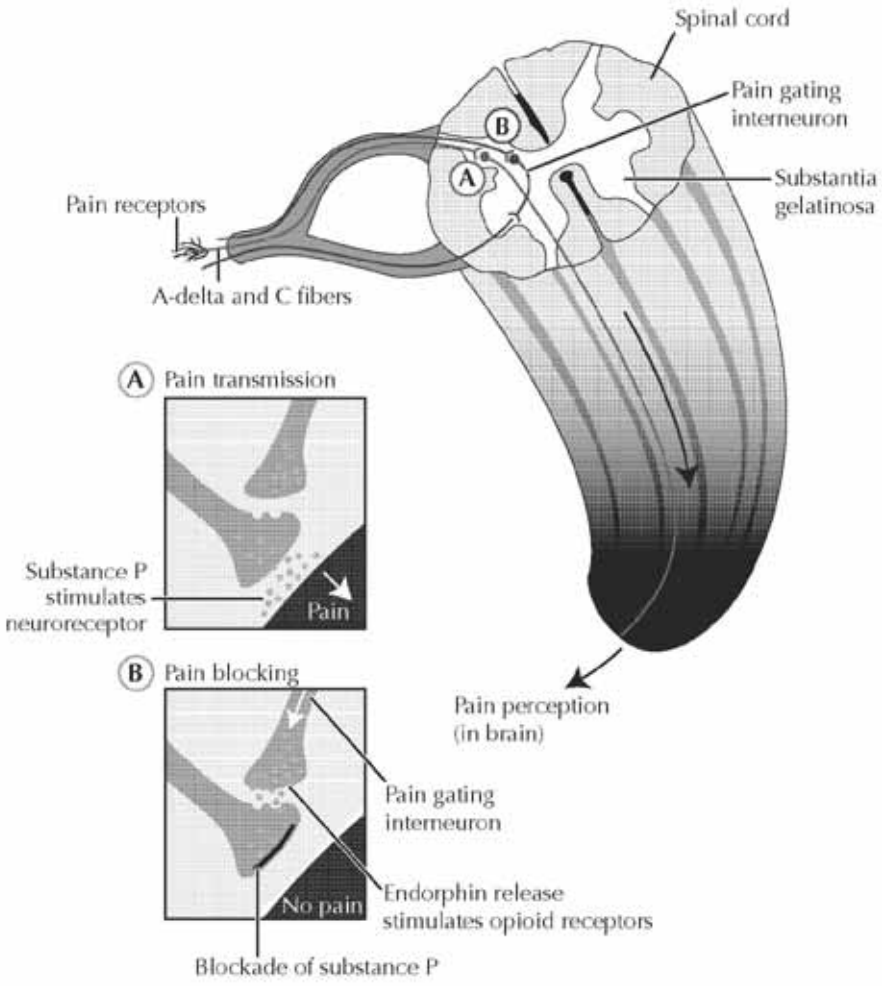
In addition to pain fibers, large diameter A-beta (Aβ) fibers carry impulses for tactile and vibratory stimulation from the skin. According to Melzack and Wall, the domination of either the touch fibers or pain fibers determines if the pain gate is open or closed. If sensory impulses along the touch fibers dominate or outnumber the pain impulses, the gate will close. This explains why massaging a painful area can decrease the intensity and duration of pain. *[Huether, 2006, 452]*

A-beta fibers carry tactile and vibratory stimuli.

If touch sensory impulses outnumber pain impulses, the pain gate closes.

FIGURE 5

Mechanism of pain transmission and blocking in the spinal cord: pain signals are usually transmitted to the brain, but may be blocked through the action of endorphin-releasing interneurons.



In addition, descending pathways from the cerebral cortex and medulla act to suppress pain.

The gate control theory also proposes that descending pathways from areas in the midbrain and brain stem act to suppress pain. It is believed that psychological/emotional and other factors act on the cerebral cortex, which then signals to the medulla. Descending signals are sent from the medulla to the spinal cord. *[Fausett, 2004, 32; Huether, 2006, 453]*

These descending pathways release **serotonin** and **norepinephrine** in cells in the gray matter of the spinal cord. Situated in the area of the substantia gelatinosa neurons are small interneurons that form inhibitory circuits (see Figure 5). These small interneurons release **endorphins** that inhibit glutamate and substance P release from the

A-delta and C fibers. The endorphins are the body's self-generated opioids that inhibit (gate) pain by acting at the **opioid receptor** to stop the release of glutamate and substance P. Besides endorphins, gamma-amino butyric acid (GABA) acts as an inhibitor on central nervous system neurons. *[Huether, 2006, 450, 452, 454–455; Woodruff, 2004, 58; Sugerman, 2006, 419]*

In the spinal cord, small interneurons form inhibitory circuits. Interneurons release endorphins that inhibit glutamate release and substance P actions.

Summary

- Transmission of pain is signaled between incoming A-delta and C fibers and the spinal neurons through the action of excitatory neurotransmitters such as glutamate, aspartate, and substance P.
- The substantia gelatinosa neurons then transmit the pain signal through the spinal cord; from there, the pain signal enters the brain through the medulla oblongata, reaches the thalamus, and is relayed to the cerebral cortex.
- Pain can be gated (blocked) in the spinal cord by intense tactile input through A-beta fibers or by activation of pathways descending from the brain into the spinal cord with psychological and emotional responses. These pathways stimulate inhibitory interneurons in the spinal cord, which release natural opioids (endorphins).
- Endorphins inhibit the release of glutamate and substance P from the excitatory A-delta and C fibers. Thus, opioid substances act to inhibit pain transmission in the central nervous system.

Review Questions (I)

DIRECTIONS. Circle the letter corresponding to the correct response in each of the following items.

1. A biochemical substance that facilitates pain but does not produce pain by application is

   a. bradykinin.
   b. histamine.
   c. prostaglandin.
   d. serotonin.

2. Which of the following is *correct* about peripheral pain fibers?

   a. A-delta fibers are covered by myelin, and conduct impulses quickly.

   b. A-delta fibers are not covered by myelin, and conduct impulses slowly.

   c. C fibers are covered by myelin, and conduct impulses slowly.

   c. C fibers are not covered by myelin, and conduct impulses quickly.

3. The *primary* excitatory nociceptive transmitter substances in the spinal cord are

   a. glutamate and aspartate.
   b. glutamate and substance P.
   c. norepinephrine and serotonin.
   d. substance P and norepinephrine.

4. Tactile input can _____ pain transmission in the spinal cord.

   a. block
   b. initiate
   c. perpetuate
   d. sensitize

5. Pain inhibitory interneurons use _____ as a transmitter.

   a. endorphin
   b. glutamate
   c. NMDA
   d. Norepinephrine

Check your responses on page 69.

II. WHAT IS PAIN?

Pain sensation serves an essential purpose, as it calls attention to disease, injury, and harmful environments, and thereby signals the person to take protection from further damage when possible. However, pain is more than an unpleasant sensation, as it engenders fear and other unpleasant human emotions. As a consequence of these psychological factors, the amount of pain is not only related to the intensity of injury, but also to the type and extent of the patient's emotional and attitudinal responses.

Pain can vary in intensity from mild, in which case it may only be a nuisance, to severe pain that demands attention. Pain is a common cause of suffering and impairs the quality of life for millions. For some the pain may be short lived, in others it may persist for weeks or months, while for others it will debilitate them for the rest of their lives. Pain is an individual health problem that has an economic impact. It must be effectively treated and managed when it is present to any significant degree.

A. Definition of Pain

Pain is an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage.

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory or emotional experience associated with actual or potential tissue damage or described in terms of such damage." While this definition creates the impression that pain is a static, unchanging experience, we will see later in this module that pain experience is actually dynamic and fluctuating. *[Huether, 2006, 448]*

Patient reports of pain should be believed.

The sensation of pain is entirely subjective and can be felt only by the patient. Pain is what the patient says it is even if no cause can be found. Thus, patient reports of pain should be believed, discussions about pain should be initiated, and the severity of pain should be evaluated and recorded. The patient is the best

authority on his or her own pain. Even if tissue damage is not obvious, pain can still exist. On the other hand, tissue damage may in some circumstances not be associated with complaints of pain. Further, psychological and cultural factors can strongly influence the impact and the expression of pain. These factors will be discussed in Section III. *[Carver, 2005, 8–9; Woodruff, 2004, 54, 56, 61; Guyton, 2006, 604]*

Psychological factors can strongly influence the impact and expression of pain.

B. Duration of Pain (Acute vs Chronic)

Pain is classified in several different ways. One of the most important of these is acute or chronic, depending on the duration of the pain. Acute pain lasts a brief period, while chronic pain persists for a prolonged period, but there is no unanimous agreement on the dividing line between "brief" and "prolonged." Some clinicians hold that acute pain lasts less than 1 month, others say that acute pain lasts less than 3 months, while some use a time frame of less than 6 months. Despite differing definitions of the time period, there is general agreement over the characteristics of acute and of chronic pain. *[Huether, 2006, 456–457; Woodruff, 2004, 59]*

Acute pain lasts a brief period, while chronic pain persists for a prolonged period.

Acute pain is usually caused by a noxious stimulus such as injury or disease, and is both a sensory and psychological experience often associated with **autonomic nervous system** responses (increased blood pressure, heart rate, and sweating). As a result of therapy or the self-limiting nature of the disease, the pain usually disappears in days, weeks, or a few months. Thus, acute pain seems to warn of tissue damage and the need for rest. An example of acute pain is the pain that follows surgery, which can be significant but often resolves gradually as the wounds heal. *[Woodruff, 2004, 59; Huether, 2006, 456–457; Willis, 2007, 16–17]*

Acute pain is usually caused by a noxious stimulus such as an injury or disease.

An example of acute pain is pain that follows surgery.

Chronic pain refers to pain that persists for months or years after the onset of an illness or injury. Chronic pain may be caused by a persistent disease, or by an abnormality of the nervous system.

Chronic pain persists for months or years after the onset of an illness or injury.

Chronic pain impairs the patient's quality of life.

While chronic pain is usually associated with a lengthy disease process, a causative factor may not be found in some patients. Chronic pain is often insidious in onset and is often characterized by fluctuations in intensity. Chronic pain serves no clear biological function, and it can profoundly impair the patient's quality of life. *[Woodruff, 2004, 59–61; Huether, 2006, 457–458; Silver, 2007, 428–429]*

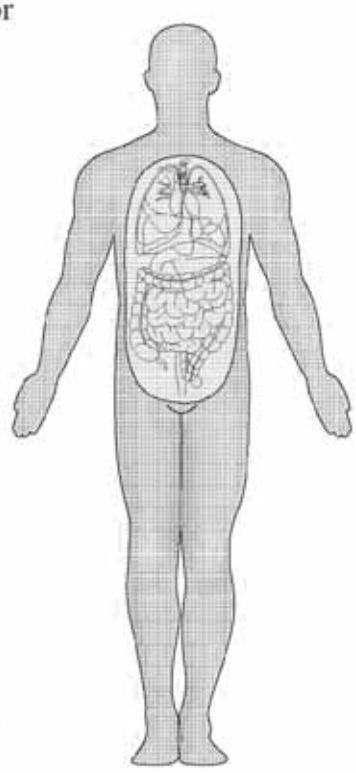
C. Types of Pain

Pain is categorized into types according to various schemes.

Pain is categorized into types according to various schemes. One of these is its anatomic/physiologic cause, while another pain categorization method is based upon its temporal persistence or transience.

There are three general pain types: somatic, visceral, and neuropathic. Somatic pain comes from nociceptors in cutaneous and deep connective tissues.

Three general types of pain are recognized based upon the underlying mechanism: somatic, visceral, and neuropathic. Somatic pain results from stimulation of specific nociceptors in **cutaneous**, subcutaneous, or deep connective tissues, such as muscles, tendons, and bones. Somatic pain is usually described as either "dull" or "sharp" and as "aching." Examples of superficial somatic pain include sunburn, chemical or thermal burns, and cuts of the skin. Examples of deep somatic pain include arthritis pain and tendonitis. *[Woodruff, 2004, 61; Huether, 2006, 456–457; NPC and JCAHO, 2001, 9]*



Visceral pain arises from injury, distention, obstruction, or inflammation of thoracic, abdominal, or pelvic organs.

Visceral pain is nociceptive pain that originates from injury, distention, obstruction, or inflammation of organs in the thorax, abdomen, or pelvis. For example, visceral pain may arise from distention or spasm of a hollow viscous (eg, bowel), ischemia (lack of blood supply), or from the rapid stretch of the capsule of a solid organ (liver). *[Guyton, 2006, 604; NPC and JCAHO, 2001, 9]*

Unlike somatic pain, neuropathic pain does not result from nociceptor stimulation, but instead is caused by either injury to or destruction of nerves. Neuropathic pain can be either peripheral or central, depending on whether the affected nerves are in the **peripheral nervous system (PNS)** or **central nervous system (CNS)**, respectively. This type of pain results in an abnormal function of the nerve, manifesting as pain which is characterized as "burning," "aching," or "tingling." Neuropathic pain may be constant and sustained, and there may be intermittent, superimposed, shock-like pain which is described as shooting or electrical. In addition, abnormal sensations may be apparent such as **allodynia**, **paresthesia**, and **dysesthesia**. *[Huether, 2006, 459; Gallagher, 2008, S2–S3]*

Neuropathic pain is caused by injury to or destruction of nerves.

Abnormal sensations may occur with neuropathic pain.

The genesis of neuropathic pain is unpredictable. The same apparent lesion may cause minimal pain in one patient while causing severe neuropathic pain in another patient. Injuries that cause neuropathic pain range from trivial to severe. Neuropathic pain has a number of different causes, such as nerve compression by a tumor, and neuroma (nerve tumor growth). Neuropathic pain may be extremely difficult to treat with standard analgesics. Table 1 presents some of the differences among somatic, visceral, and neuropathic pain. *[Cervero, 2003, 31; Huether, 2006, 460; Gilron, 2006, 265–266]*

Neuropathic pain may be extremely difficult to treat with standard analgesics.

Characteristic	Somatic Pain	Visceral Pain	Neuropathic Pain
Origin	Stimulation of nociceptors	Stimulation of nociceptors	Nerve damage
Nerve function	Normal	Normal	Abnormal
Location of injury	Tissue (skin, muscle, tendon, bone, etc.)	Abdominal, thoracic, pelvic viscera	Nerves
Descriptions	Dull, sharp, aching, gnawing	Dull, aching, colicky, referred to cutaneous sites	Burning, shooting, tingling
Abnormal sensations	None	None	Common
Response to analgesia	Tends to respond	Tends to respond	Poor response
Examples	Injury, postoperative pain, bone cancer pain	Pancreatic cancer pain, liver/lung cancer pain	Herpes zoster neuralgia, phantom limb pain, tumor invasion of nerves

TABLE 1

Comparison of characteristics of somatic, visceral, and neuropathic pain: different types of pain vary in their origin, nerve involvement, and description, among other traits.

Another way of differentiating types of pain is according to temporal characteristics. In this scheme, pain is categorized according to its persistent or transient nature, as follows:

Persistent pain is pain that is always present; it should be treated by around-the-clock analgesic dosing.

1. Persistent Pain. Pain that has been present day after day for at least 6 months is known as persistent pain. It should be treated by **around-the-clock (ATC)** dosing of pain medication to maintain a relatively constant level of pain relief. This means giving long-acting medication at fixed times. *[Payne, 2007, S1, American Cancer Society, 2007, 7]*

Breakthrough pain is a transitory flare of pain of at least moderate intensity over an ongoing, persistent pain in patients receiving chronic opioid therapy.

2. Breakthrough Pain. Breakthrough pain occurs on a background of otherwise controlled persistent pain; it is distinct from uncontrolled pain. Breakthrough pain is described as a transitory exacerbation or flare of moderate to severe pain in patients with otherwise stable persistent pain who are receiving chronic opioid therapy. In one study, the median duration of breakthrough pain was about 60 minutes. Breakthrough pain tends to be the most intense pain. Figure 6 illustrates this type of pain. *[Payne, 2007, S3; Portenoy, 2006, 586; Davis, 2004, 629]*

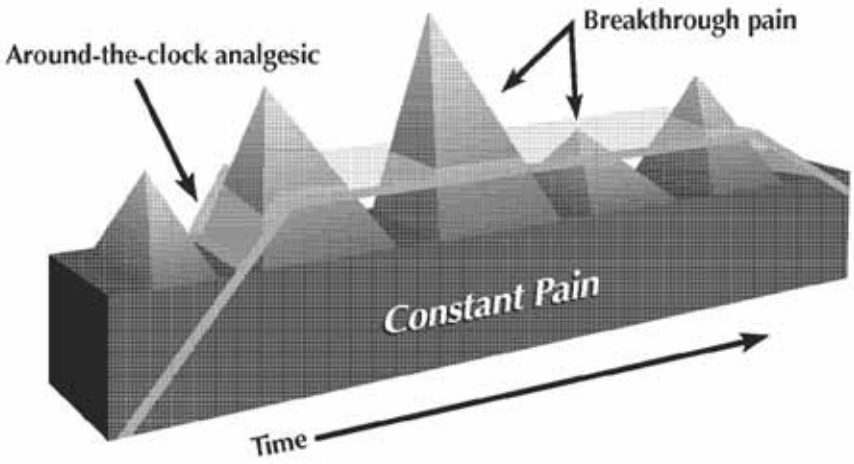


FIGURE 6

Breakthrough pain episodes on a background of persistent pain; while an around-the-clock analgesic can manage constant pain, flares of breakthrough pain appear despite regular analgesic dosing.

There are three subtypes of breakthrough pain: *[Payne, 2007, S4]*

The three subtypes of breakthrough pain are incident, end-of-dose failure, and spontaneous.

- **incident pain**
- **end-of-dose failure pain**
- **spontaneous/idiopathic pain**

Incident pain is precipitated by an identified event, such as the patient's coughing or walking. End-of-dose failure pain occurs at the end of the regular dosing interval (eg, pain occurring 10–11 hours after a medication dosed every 12 hours) and may be managed by adjusting the dose or frequency of the ATC medication. Finally, spontaneous/idiopathic pain has no identified precipitating event and no relation to medication timing. Breakthrough pain is often managed by adding a medication in addition to the drug used for the persistent pain. *[Payne, 2007, S4–S5; Duragesic, 2008, 1]*

Incident pain is precipitated by an identified event.

End-of-dose failure pain occurs at the end of the regular dosing interval.

Spontaneous/idiopathic pain has no identified precipitating event.

3. Intermittent pain. This is pain that is unpredictable in onset and duration, (eg, pain resulting from kidney stones). Unlike breakthrough pain, there is no baseline of chronic or persistent pain. Pain that is unpredictable in onset requires treatment with an analgesic on an as-needed basis. An opioid with rapid onset and short duration may be appropriate for managing intermittent pain. *[Duragesic, 2008, 2; START, 2008, 1]*

With intermittent pain, there is no baseline of persistent pain.

D. Location of Pain

Somatic pain arises from nociceptive stimulation. It may be superficial or deep. When skin and other superficial nociceptors are stimulated, the pain is usually sharp and well localized. Pain that arises from deep nociceptors, such as in muscle or tendons, may be sharp or dull and less clearly localized. *[Huether,2006, 448; Woodruff, 2004, 61]*

Somatic pain may be superficial or deep.

Pain localization is best in skin regions.

Visceral pain is often associated with a phenomenon called referred pain. Instead of reporting the pain as originating from the area around a specific organ, the patient reports it as arising from a distant site. Examples of this are neck, shoulder, and arm pain that occurs with heart disease, and shoulder pain from liver or diaphragm disease or injury. The nerves that convey sensation from the viscera comprise only about 10% of all the fibers that reach the spinal cord. These visceral nerve fibers end on the same nerve cell that receives other information, such as from skin. This may explain why pain is felt as referred pain. *[Guyton, 2006, 603–604; Giamberardino, 2005, 3; Huether, 2006, 457–458; Carver, 2005, 7; Willis, 2007, 2617]*

Referred pain is visceral pain reported as arising from a site distant from the actual source of pain.

The distribution of abdominal and pelvic pain is vague.

When visceral pain is not referred, the distribution is vague and described as deep, vague, aching, or pressure-like. It is often accompanied by changes in blood pressure, heart rate, nausea, vomiting, and sweating. Only when somatic structures are involved does the pain pattern become more specific. *[Huether, 2006, 457; Giamberardino, 2005, 2–3; Willis, 2007, 2615]*

Some patients have more than one pain area, and it is necessary to obtain information about each of the individual sites of pain. Locations and intensity of pain may be indicated on a body diagram. *[Davis, 2004, 628; Locker, 2008, 82]*

E. Severity of Pain

Pain severity is subjective.

The simplest way to describe severity is as mild, moderate, or severe.

By the definition of pain, the severity of pain is how intense the patient says it is. There is no objective measure of pain severity, and the health team has to rely on the patient's report. While certain instruments can measure the intensity of the patient's pain, they only help to document its subjective intensity. The simplest instrument describes pain severity as mild, moderate, or severe. *[Carver, 2005, 7; Willis, 2007, 1644; McLafferty, 2008, 42–45]*

When clinicians need a more detailed description of the patient's pain, they will use pain **rating scales**. These instruments use numbers, descriptive words, and combinations of numbers and words to describe pain intensity. The intensity of pain can be assessed in children and nonverbal patients using other forms of pain scales like the Faces Pain Scale. The Faces Pain Scale depicts six faces from a sad, crying face to a happy, smiling face. Use of these scales is described in greater detail later in this module. However, pain is a complex experience rather than a simple sensation that can be described by a number. Therefore, many other dimensions of pain need to be assessed, as well as other patient and disease factors. *[Carver, 2005, 7; Willis, 2007, 1644; McLafferty, 2008, 42–45]*

Rating scales provide more detailed descriptions of a patient's pain.

Summary

- Pain may be a component of actual tissue damage or may be an experience described in terms of such damage.
- Pain is a subjective experience, with the patient as the primary source of information.
- Pain can either be acute or chronic in duration. Acute pain has an immediate onset following injury or disease, while chronic pain persists for prolonged periods, with no agreement on where to draw the dividing line.
- Somatic pain results from stimulation of nociceptors because of tissue injury or disease, and pain varies from dull to sharp and from superficial to deep.
- Visceral pain results from stimulation of nociceptors in visceral organs, is often dull in nature, and may be referred to other locations.
- Neuropathic pain is caused by disease or injury of the nerves, resulting in a variety of unusual burning, shooting, and tingling sensations, as well as other abnormal sensations.
- While persistent pain is always present, breakthrough pain appears against a background of otherwise controlled persistent pain.
- Breakthrough pain is a transitory exacerbation or flare of moderate to severe pain in patients with otherwise stable persistent pain who are receiving chronic opioid therapy.

Review Questions (II)

DIRECTIONS. Circle the letter corresponding to the correct response in each of the following items.

1. In the literature on pain, there is general agreement that

   a. acute pain lasts less than 1 month.
   b. chronic pain lasts more than 5 weeks.
   c. open heart surgery causes acute pain.
   d. open heart surgery causes chronic pain.

2. Liver disease causing pain felt deep within the body is _____ pain, while liver disease causing shoulder tip aching is _____ pain.

   a. neuropathic; referred
   b. neuropathic; visceral
   c. visceral; referred
   d. visceral; somatic

3. Which of the following statements about neuropathic pain is *correct?*

   a. Burning, shooting, and tingling sensations are typical.
   b. Dull, sharp, and aching sensations are typical.
   c. It responds well to analgesics.
   d. It results from nociceptor stimulation.

4. Which statement about pain severity is *correct?*

   a. Blood pressure provides an objective measure of severity.

   b. Heart rate provides an objective measure of severity.

   c. Rating scales document pain's objective intensity.

   d. Rating scales document pain's subjective intensity.

Check your responses on page 69.

III. EVALUATION OF PAIN

Patients presenting to physicians with complaints of pain should be carefully evaluated. Pain assessment is critical in diagnosing the underlying disease, following disease progression, and selecting and evaluating treatment. In certain diseases such as cancer, evaluation of pain is ongoing; it is part of the patient's routine management. Pain is reassessed following initiation of treatment and is periodically reevaluated as part of a treatment plan or upon evidence of disease progression. The World Health Organization has published the following guidelines for cancer pain evaluation that apply to most pain patients: *[WHO, 1996, 8–11]*

- believe the patient's report
- initiate discussion of pain
- evaluate degree of pain
- take a detailed history
- evaluate the patient's psychiatric condition
- perform a physical exam
- order any necessary tests or diagnostic procedures
- consider alternative methods of pain relief
- monitor treatment results

A. Patient Pain History

Assessing pain requires good patient rapport.

Pain is a subjective and an individual experience that an observer cannot estimate. Assessing pain appropriately requires good patient rapport, since patient self-report is the primary source of information about pain. Further, patients are often hesitant to volunteer information about pain, so health care professionals must therefore ask about pain. Several studies have also shown that physicians consistently underestimate patients' physical pain and overestimate psychological components associated with the symptom. This causes a clinical concern, because inadequate pain management occurs more commonly when patients and

Studies have shown that physicians underestimate patients' physical pain.

physicians differ in their judgment of the pain's severity. The patient's description of pain is the key element of any assessment. *[Carver, 2005, 9; Woodruff, 2004, 54; Gunnarsdottir, 2003, 421; Brennan, 2007, 208]*

Proper pain assessment has several benefits. First, an initial assessment should establish a rapport with the patient. The patient's trust may enhance communication regarding active treatment and pain management. *[NPC and JCAHO, 2001, 21; Carver, 2005, 9]*

A proper pain assessment establishes trust in the health care provider.

Second, pain may be associated with disease progression, so pain assessment may provide information that can guide cancer therapy. Changes in pain characteristics may signal disease progression or complication. Pain in new areas may lead a clinician to conduct appropriate diagnostic tests. *[Davis, 2004, 628, 631]*

Changes in pain may signal changes in the underlying disease.

Third, frequent pain reassessment will help gauge the effectiveness of analgesic therapy. Assessment may help health care professionals choose more effective agents, titrate the dose or dosing interval appropriately, check the usefulness of the current route of administration, manage side effects, and assess the need for more effective breakthrough pain medication alongside the around-the-clock medication. *[Carver, 2005, 10–11; McCarberg, 2007, S8]*

Frequent pain assessment guides changes in analgesic therapy.

In assessing pain, physicians review several key components of the pain, including exacerbating/relieving factors, quality, location and spread, intensity or severity, and timing. Some use the mnemonic "PQRST" to remember these components of the pain history: *[McLafferty, 2008, 46]*

The mnemonic PQRST stands for precipitating factors, quality, region or radiation, subjective description, and temporal nature; all of these are important to understand the patient's pain.

- P (precipitating factors): what causes the pain or makes the pain better or worse?
- Q (quality of pain): what does the pain feel like?
- R (region or radiation of pain): is the pain in one place only, or does it radiate anywhere else?

- S (subjective description of pain): how severe is the pain on a scale of one to 10?
- T (temporal nature of pain): when did the pain start and how long did it last?

The clinician will also ask questions about what drugs the patient has taken, whether they have relieved the pain, and how well the medication is tolerated. Additionally, the clinician should ask about how well the patient is sleeping, and about the patient's limitations on activity or function. The clinician may also ask about anxiety and depression, which may contribute to pain and which may need to be treated. *[Carver, 2005, 9]*

B. Physical Examination

The physical exam includes observation of the patient, vital signs, and nonverbal behaviors.

After taking the history, the next step is to perform a physical assessment—observing the patient for physical signs of the source of pain. Nonverbal behaviors, like cradling the arm, may be indictors of pain. Physiologic responses such as vital signs are routinely assessed and fluctuations may be related to pain. However, because abnormally high or low vital signs may be present when the patient is complaining of pain, they are not reliable indicators of pain when used without supporting assessment data. A complete musculoskeletal and neurological examination may be needed. The neurological examination will detect any sensory deficits or neuromuscular weakness. *[Carver, 2005, 10; Huether, 2006, 458; Dunwoody, 2008, S20–S23]*

The exam may also include a musculoskeletal and neurological exam.

Additional tests may be requested, such as x-rays, CT, MRI, and EMG.

Although the source of pain is usually diagnosed by the patient history and exam, additional medical tests may be necessary. These are typically done by referral to diagnostic centers and/or hospitals. Laboratory tests may help determine disease progression. X-rays allow visualization of bone integrity, but not of soft tissue and organ pathology. **Computerized tomography (CT)** and **magnetic resonance imaging (MRI)** scans can visualize

internal organs and allow the physician to detect soft tissue abnormalities, tumors, injuries, and other physical sources of pain. **Electromyographic (EMG)** recording allows the clinician to examine the function of muscle groups, and assess for abnormal activity that may be related to somatic/muscular pain. *[Carver, 2005, 10]*

C. Pain Rating Instruments

One-dimensional pain rating scales were previously introduced. They allow some measurement of the subjective pain experience and evaluate the effectiveness of treatments. A commonly used tool is the Visual Analog Scale (VAS). The VAS consists of a horizontally divided line 10 cm long with a label of "no pain" on the left side and "pain as bad as it could be" as a label on the right side. The patient is instructed to mark the place on the line that best represents their pain. The VAS gives reliable and reproducible data but does not directly provide numeric data. The Verbal Graphic Rating Scale (VGRS) is a modification of the VAS scale that uses simple descriptive phrases about the pain's intensity. The Numeric Rating Scale (NRS) is another related scale in which the patient is asked to select a number between 0 and 10 to describe the level of pain, with 0 representing no pain and 10 representing pain as bad as it could be. This NRS also gives reliable and reproducible information. Variations of these scales for children substitute gradations of smiling to crying faces for the numbers. All four scales are illustrated in Figure 7 on the next page. *[Carver, 2005, 9; Dunwoody, 2008, S18–S19; McLafferty, 2008, 44–46]*

The VAS consists of a horizontal 10-cm line with labels of "no pain" on the left side and "as bad as it could be" on the right.

The NRS uses number from 0 to 10 for pain ratings.

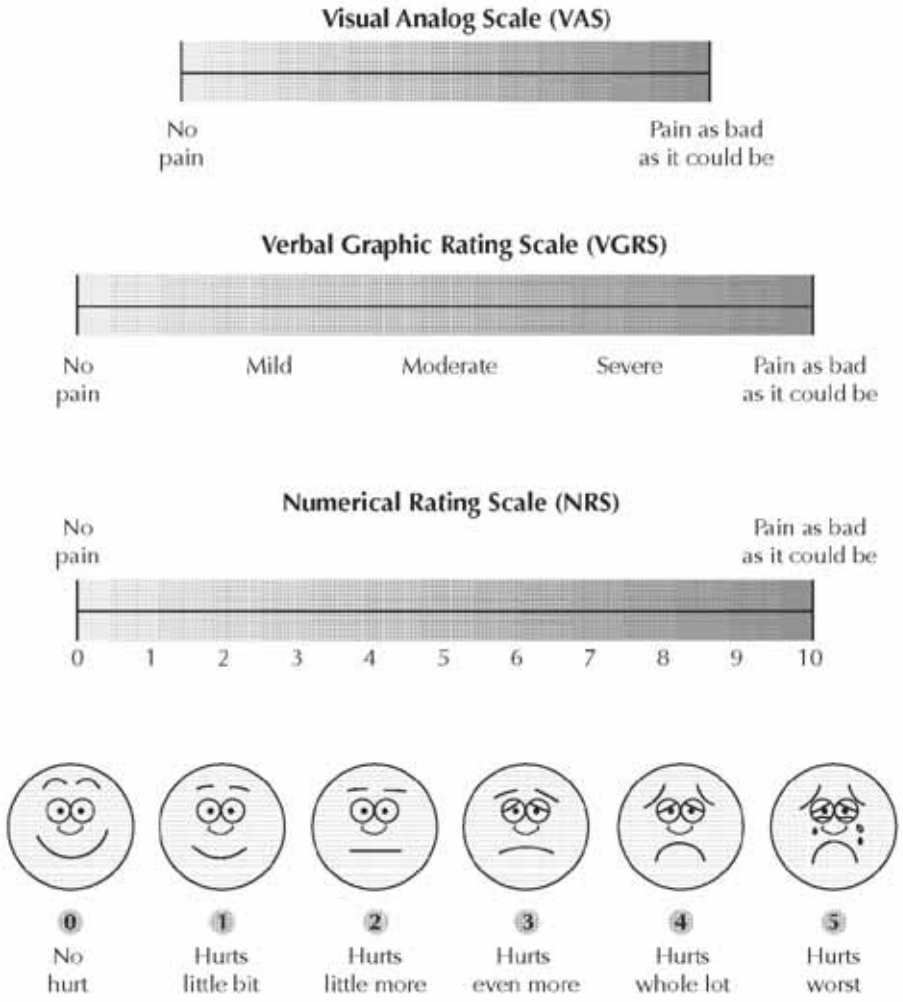
The McGill Pain Questionnaire (MPQ) is a more extensive, multidimensional rating instrument. In addition to pain intensity, it assesses duration, type, and quality of pain, any precipitating or relieving factors, and the presence of clinical depression. Patients choose from a list of 78 adjectives that evaluate the sensory, emotional, and affective elements of their pain. The MPQ also includes a schematic representation of the body that is shaded by the patient to indicate the location of the pain. This questionnaire

The McGill Pain Questionnaire is a more in-depth rating instrument.

has been extensively tested and is commonly used to evaluate cancer pain. *[McLafferty, 208, 43–44; Dunwoody, 2008, S20; NPC and JCAHO, 2001, 28; Davis, 2004, 627]*

FIGURE 7

Pain intensity scales: a variety of pain intensity rating scales are available for clinical use.



The Brief Pain Inventory and Memorial Pain Assessment Card are also used for pain evaluation.

Brief Pain Inventory (BPI) and Memorial Pain Assessment Card are multidimensional assessment tools that take less time to administer than the MPQ. The BPI uses a numeric scale and 11 questions to evaluate intensity of pain and its effects on the patient's life. The Memorial Pain Assessment Card uses a VAS to assess pain intensity, pain relief, and mood. *[McLafferty, 208, 44; Dunwoody, 2008, S20]*

D. Factors Affecting Pain Reporting

Patient self-report of pain is the most important means of assessing pain, yet patients may be reluctant to report pain. A study of physicians in the Eastern Cooperative Oncology Group (ECOG) found that health care providers ranked patient assessment as the most difficult barrier to treating cancer pain, with patient reluctance to report pain ranked second as an issue. Because pain often increases with progressing disease, patients may fear that admitting that they have increasing levels of pain is admitting that the prognosis is getting worse. Further, patients may fear "distracting" a doctor from the active cancer treatment plan. *[Carver, 2005, 8; NCI, 2008b, 1; Willis, 2007, 214, 261]*

Patients may be reluctant to report pain.

Patients may fear that increasing pain means worsening prognosis.

Patients may fear "distracting" the doctor with pain complaints.

Patients can also inhibit therapy by refusing to take pain medications or by taking them inappropriately. Patients may hear descriptions of **physical dependence** about certain medications (opioids) and fear the stigma or behaviors they associate with drug addicts—behaviors that are not common in patients without previous history of **addiction**. Patients may believe that analgesics should be "saved" until the end of life so that they are effective then; patients may need reassurance that an appropriate dosage of opioid will be available as pain increases, and they need not suffer now to avoid analgesic **tolerance** in subsequent disease stages. *[Carver, 2005, 10–11; Gunnarsdottir, 2003, 426; Willis, 2007, 261]*

Patients may fear the stigma or behaviors they associate with drug addicts.

Patients may believe that analgesics are only for those near death.

Because of stoic personal attitudes towards pain or because of cultural or religious dispositions toward suffering or legitimate drug use, some patients may need reassurance to use analgesics at all. Still others may need reassurance that side effects associated with analgesic use will be managed. Some patients suffer in silence because they are trying to be good patients or do not want to bother anyone. Others think that nothing can be done anyway and if they complain the clinician will lose focus on their medical

Patients may need reassurance that it is all right to use analgesics.

problem. These are just a few of the factors affecting patient pain reporting. Thus, patient-clinician rapport and trust are cornerstones to successful pain management. *[National Cancer Institute, 2008, 1; Gunnarsdottir, 2003, 426; Willis, 2007, 262]*

Caregivers may lack information about the benefits of proper pain management and may have misconceptions about opioids.

Family members/caregivers may worsen patient concerns and fears about analgesic use. Caregivers may lack information about proper pain management and its benefits. Like patients, caregivers may need reassurance that few people using opioids for a legitimate medical reason become addicted to the drug, and that physical dependence to a drug is easily overcome through scheduled dosing decreases, if the patient improves to the point where opioids are no longer needed. Because caregivers play an integral role in therapeutic success, it may be helpful for health care providers to educate both patients and their caregivers about pain management programs in a joint discussion. *[Willis, 2007, 261–262; AACPI, 2004, 6–7]*

Both patients and caregivers need pain management education.

Summary

- Pain assessment involves the use of a set of questions focusing on the history of the symptom(s), with or without use of pain rating scales.
- Simple scales commonly used include the Visual Analog Scale, the Verbal Graphic Rating Scale, and the Numeric Rating Scale. More thorough instruments include the McGill Pain Questionnaire, the Brief Pain Inventory, and the Memorial Pain Assessment Card.
- The physical examination for pain usually includes recording of vital signs, observation of nonverbal behaviors, and musculoskeletal and neurological examinations.
- Additional medical tests that may be requested when warranted include the CT scan, MRI scan, x-ray, and EMG recording.
- Whatever the skill of the clinician, an accurate pain assessment will depend upon the patient's accuracy and completeness of reporting.
- Many factors inhibit full reporting, and these include fear of admitting the pain, fear of distracting the doctor from the cancer/disease, fears of addiction and dependence, stoic attitudes, cultural/religious dispositions, the wish to be a model patient, and psychological denial.
- To address these factors and engage the patient in proper pain therapy, there must be rapport and trust between the patient and the clinician.

Review Questions (III)

DIRECTIONS. Circle the letter corresponding to the correct response in each of the following.

1. Which of the following is **not** a benefit/result of a proper pain assessment or reassessment?

   a. diagnostic clues on disease progression

   b. enhanced communication regarding treatment and pain management

   c. evaluative data on effectiveness of analgesic therapy

   d. quantitative data on substance P levels in spinal cord

2. The mnemonic _____ is used by clinicians to remember factors included in the pain history.

   a. HISTR
   b. MNNOP
   c. PQRST
   d. QUEST

3. Once the initial examination has been completed, additional medical tests done by referral may include

   a. CT, EMG, MRI, and x-ray.
   b. CT, EMG, nonverbal behaviors, and x-ray.
   c. EMG, MRI, nonverbal behaviors, and vital signs.
   d. MRI, x-ray, and vital signs.

4. Which of the following is a pain rating scale?

   a. BPI
   b. MPQ
   c. VAS
   d. all of the above

5. Which of the following is likely to influence a patient's pain reporting?

   a. cultural/religious disposition
   b. fear of addiction
   c. stoic attitude
   d. all of the above

Check your responses on page 69.

IV. ISSUES IN PAIN MANAGEMENT

Historically, medical therapy has emphasized diagnosis and treatment of medical and surgical problems. Pain and patient suffering took a back seat until the 1990s. Organizations such as the World Health Organization pioneered pain care policy. In the 1990s, the United States Agency for Health Care Policy and Research (AHCPR), published the first clinical practice guideline for pain management. JCAHO recently added new standards on pain into its accreditation standards. These require that health care facilities and organizations integrate pain assessment and management into patient care routines. Further, in 2001, the American Cancer Society issued cancer pain treatment guidelines for patients, and in 2005 the American Pain Society made available evidence-based clinical practice guideline for pain management in cancer. These and other professional organizations now recognize that untreated pain can cause needless suffering, impair patients' ability to function, and increase the burden on their families. Nevertheless, pain continues to be undertreated. *[de Leon-Casasola, 2008, S3; NPC and JCAHO; 2001, 3; ACS, 2001, 1; APS, 2005, 1]*

A. Undertreatment

Undertreatment of pain is frequent, due to factors related to:

- health care professionals
- patients
- the health care system

Physicians may undertreat pain due to a lack of pain education.

Health care professionals may also be inadequately educated about pain.

1. Factors Related to Health Care Professionals. Physicians often undertreat pain due to a lack of education about pain. This results in an inadequate pain assessment and less than optimal treatment, such as use of nonsteroidal analgesics for severe pain. Some health care professionals have often been inadequately prepared to care for patients with pain. Medical textbooks and courses

provide insufficient coverage of pain management. *[Gunnarsdottir, 2003, 419–422]*

Health care professionals also have concerns and fears about opioid side effects and fears about addiction. The actual likelihood of becoming addicted to opioids when used under medical supervision varies by patient population. Factors that increase the likelihood of developing an addiction include preexisting addictive disorders, untreated psychopathology, or a family history of addictive disease. However, in patients without personal or family history of substance abuse, addiction resulting from exposure to opioid therapy is uncommon. In one survey of patient taking opioids for severe chronic pain, only four of 11,882 patients developed addiction. *[APA, 2005, 2]*

The likelihood of a cancer pain patient becoming addicted to opioids is small.

2. Factors Related to Patients and Caregivers. Despite standards and guidelines requiring patient participation in treatment planning, patients rarely participate in a meaningful way in how their pain is managed. This may be due, in part, to patients' reluctance to discuss pain or deny their pain. Patients may also fail to adhere to a pain medication schedule. Perhaps their greatest fears, also shared by their families, are of addiction or being thought of as an addict. Other concerns of patients and their caregivers include: *[AACPI, 2004, 6–7; Reyes-Gibby, 2007, 261]*

Patients often lack information on pain management options.

Patients and their families are often fearful of addiction and tolerance.

- pain medications shorten life
- admitting pain is equivalent to weakness
- side effects of pain medicine are worse than the pain itself

3. Factors Related to the Health Care System. Another significant barrier to appropriate opioid pain management is concern over the legal liabilities associated with controlled substances. The federal Controlled Substances Act categorizes drugs with potential for abuse and controls their manufacture and distribution. Numerous federal and state laws, rules, and regulations guide the prescribing of controlled substances, such as opioids. Physicians suspected of

Monitoring of opioids by regulatory agencies may inhibit their prescription.

inappropriate or excessive prescribing of controlled substances are subject to investigation, disciplinary action, and prosecution. Of physicians responding to a survey, 26% said they were hesitant to prescribe opioids for patients with chronic pain for fear of being investigated by the Drug Enforcement Agency (DEA). There have been several high-profile cases recently of doctors losing their licenses due to alleged excessive prescription of opioids for pain management. *[Pain & Policies Study Group, 2008, 1; APA, 2005, 2–4; Brennan, 2007, 209]*

Lack of knowledge about controlled substance regulation can prevent pharmacists from stocking and dispensing opioids.

Pharmacists share responsibility with physicians for the legitimate use of opioids and are also subject to regulation of controlled substances. Lack of knowledge and understanding of regulations prevent other pharmacists from filling prescriptions. In one survey, 17% of pharmacists reported not stocking opioids because they are concerned about being investigated. Pharmacists also fear robbery and many pharmacies do not stock opioids for that reason. *[APA, 2005, 2–4]*

Many cancer patients are uninsured or underinsured.

Many patients with cancer are uninsured or underinsured. Even patients with apparently adequate insurance may have reimbursement difficulties. Reimbursement may be inadequate and the most appropriate treatment may not be reimbursed or may be too expensive for the patient. *[NPC and JCAHO, 2001, 16; National Cancer Institute, 2008; 2]*

JCAHO evaluates and accredits more than 15,000 health care organizations and programs in the US.

4. JCAHO Guidelines Address Undertreatment. JCAHO is a professional oversight body whose mission is to improve continually the safety and quality of care provided to the public by surveying and accrediting health care facilities. JCAHO evaluates and accredits more than 15,000 health care organizations and programs in the US. This accreditation allows health care organizations to be eligible for third-party reimbursement. *[The Joint Commission, 2008, 1; APS, 2000, 1]*

In 1999, JCAHO recognized pain management as an area that needed to be addressed. In 2000, JCAHO and the American Pain Society called a Leadership Summit on Pain Management, which helped to formulate the direction of new initiatives in this area. These initiatives included new standards for pain management that went into effect in 2001; health care facilities are now scored for compliance with these standards. *[Dahl, 2000, 1; APS, 2000, 1]*

JCAHO initiatives included new pain management standards that went into effect in 2001.

Organizations such as hospitals and facilities providing ambulatory care, behavioral health care, home care, hospice care, and long-term care are subject to on-site surveys by JCAHO. The pain management standards are extensive, but their intent can be summarized in the following: *[The Joint Commission, 2008,1; APS, 2000, 1; Dahl, 2001, 2]*

The pain management standards are extensive and include the following.

- Patients have a right to a complete assessment of pain and its nature and intensity. Findings should be recorded in a way that facilitates regular reassessment and follow-up.

Patients have a right to a complete assessment of pain and should be educated about effective pain management.

- Patients should be educated about effective pain management.
- Discharge planning should take into account the patient's pain needs at the time of discharge.

Patient's pain should be taken into account while planning discharge.

- Health care organizations should collect data that provide feedback about the effectiveness and appropriateness of pain management.

Health care organizations should collect data that provide feedback about performance.

B. Tolerance, Physical Dependence, and Addiction

As tolerance develops, adverse effects of a fixed drug dose may diminish. The possible exception may be constipation.

Tolerance refers to the decrease in the effects of a drug over time or the need to increase the drug dose over time to maintain a given pharmacologic effect. Any patient who requires dose escalation without disease progression or whose opioid adverse effects may disappear with repetitive dosing has evidence of tolerance. *[NPC and JCAHO, 2001, 17; ACS, 2008, 16]*

Tip:
Constipation, an adverse effect associated with many opioids, may not diminish as tolerance develops.

Physical dependence is characterized by the development of withdrawal after reducing/stopping opioid dosing.

Physical dependence is characterized by the development of a withdrawal symptoms after reduction or cessation of dosing, or administration of an opioid antagonist. Typical withdrawal symptoms include anxiety, craving, insomnia, sweating, chills, and diarrhea. Patients receiving opioids for prolonged periods usually become physically dependent. Symptoms of physical dependence are easily prevented by tapering the opioid dose instead of stopping it abruptly if discontinuing opioid therapy. *[NPC and JCAHO, 2001, 17; AACPI, 2004, 6]*

Physical dependence symptoms are preventable by tapering the opioid dose.

Both tolerance and physical dependence differ from addiction, which is a neurobiological disease with genetic, psychosocial, and environmental factors. Mood change and euphoria are effects of opioid antagonists, and persons who become addicted find this euphoria so rewarding that they abuse opioids despite harmful consequences. Addiction can be described using the four **C**s: *[NPC and JCAHO, 2001, 17; Kahan, 2006, 1082]*

*Addiction can be described as loss of **C**ontrol, continued use despite harmful **C**onsequences, **C**ompulsion to use, and **C**raving.*

- loss of **C**ontrol over use
- continued use despite knowledge of harmful **C**onsequences
- **C**ompulsion to use
- **C**raving

Pain appears to reduce the euphoric effects of opioids, so people taking opioids to manage their pain may be at a lower risk for addiction. *[APA, 2005, 2]*

Certain behaviors are sometimes mistaken for addiction. If patients receive inadequate pain relief, they may exhibit drug-seeking behaviors. This is called pseudoaddiction. When these patients receive adequate pain management, they no longer exhibit the same behaviors. Patients in pain do not usually become addicted to opioids. *[Kahan, 2006, 1082–1083; NPC and JCAHO, 2001, 17]*

When pain is not adequately managed, patients may exhibit pseudoaddiction.

Summary

- Pain undertreatment is frequent, and is due to a variety of professional, patient, and systemic factors.
- Professional barriers to adequate treatment include lack of pain management education, fears of opioid side effects, fears of addiction, and concern over legal liabilities regarding the prescribing and dispensing of controlled substances.
- Patient barriers to adequate pain treatment include fears of addiction, fears of tolerance and dependence, associations of opioid use with worsening disease, reluctance to report pain, and pain denial.
- Systemic barriers include regulatory review of physician opioid prescribing, pharmacy opioid dispensing, and inadequate health insurance reimbursement for pain medication.
- Because tolerance may occur during opioid use, doses should be adjusted to manage pain.
- Both tolerance and dependence differ from addiction (a behavioral problem involving the compulsive use of drugs for effects such as euphoria, rather than for pain control).

Review Questions (IV)

DIRECTIONS. Circle the letter corresponding to the correct response in each of the following items.

1. Which of the following is **not** an identified factor adversely affecting cancer pain management?

   a. concerns over regulatory monitoring of opioid prescriptions

   b. nursing staff's inadequate education about pain management

   c. physicians' fears of patient addiction

   d. quality assurance standards

2. The Joint Commission guidelines for pain management in accredited facilities include all of the following, **except** that

   a. health care organizations should collect data to determine the effectiveness of pain management.

   b. patients have a right to appropriate assessment of pain.

   c. patients must be provided with low-cost medications.

   d. patients should be educated about pain and its management.

3. Six months after initial diagnosis and after their cancer is believed to have been stabilized, a patient's daily morphine requirement increases from 20 mg to 60 mg in the 6 months after cancer diagnosis. This is most likely due to

   a. addiction.
   b. disease progression.
   c. physical dependence.
   d. tolerance.

Check your responses on page 69.

V. CANCER PAIN

Cancer is the abnormal, uncontrolled growth of cells, leading to the formation of tumors, or masses of cells that create space-occupying lesions in the body. Tumors may be benign or malignant, but either may disrupt body function by creating pressure on normal tissues, obstructing the pathways of body fluids and contents, and ultimately, by causing cell death of normal body tissues (see Table 2). These are some of the same mechanisms by which tumors cause pain.

Cancer Type	Pain Source	Pain Manifestation[a]
Skin (nonmelanoma)	Tissue damage	Localized, sharp, prickling, or burning
	Cancer treatment	Pain manifestation depends on type of treatment
Lung (including bronchus)	Skeletal metastasis	Localized pain
	Pancoast tumor (superior pulmonary sulcus tumor)	Pain in shoulder and arm Severe, unrelenting; worsened by arm movement
	Chest wall disease (especially thoracic tumor location)	Localized with cutaneous hyperalgesia (sharp, prickling, or burning)
	Cancer treatment	Pain manifestation depends on type of treatment
Prostate	Bone metastasis	Continuous, dull, aching
Breast	Bone metastasis	Continuous, dull, aching
	Cancer treatment	Paresthesia, dysesthesia, allodynia, hyperalgesia (related to surgery)
Colon/rectal	Pressure on bones/nerves/organs near colon	Dull, achy, gnawing, diffuse, crampy
	Cancer treatment	Pain manifestation depends on type of treatment

[a] Pain manifestation will vary depending on the individual, source of pain, and, in the case of cancer treatment, type and extent of treatment.

TABLE 2

Characterization of cancer pain: pain associated with the most common types of cancer (based on number of new cases) results from a variety of sources and is manifested in diverse ways. *[Fitzgibbon, 2001, 624; Joyce, 2008, 62; De Conno, 1996, 26; NCI, 2008a, 1–2; Prostate Cancer Foundation, 2008, 1–2; Burton, 2007, 191]*

Cancer is diagnosed in over one million Americans annually, and about 1.8 million Americans with cancer or a history of cancer were alive in January 2004. At the time of diagnosis and at intermediate stages, it is estimated that 30% to 40% of patients have moderate-to-severe pain. For patients receiving active anticancer treatment, 40%–70% have this level of pain, as do more than two thirds of patients with advanced or terminal cancer. *[ACS, 2008, 1; Woodruff, 2004, 54]*

A. What is a Malignancy?

Features of cancer include its origin from changes in one cell, improper differentiation and growth, and capacity for movement.

Cancer is a disease characterized by several features. *[Kumar, 2005, 272]*

- Cancer can begin with a malignant change to a single cell (transformation).
- Cancer cells have abnormal **differentiation** (anaplasia) and growth (dysplasia).
- Cancer cells invade surrounding tissue (local invasion) and can spread to distant parts of the body (metastasis).

Metastatic cancer has spread to other parts of the body.

Cancer is considered localized if it has not spread beyond the tissue or organ in which it is growing and **metastatic** if it has spread to other parts of the body. All cancers can correctly be called tumors, but not all tumors are cancers. In the field of **oncology**, the word **neoplasm** is used interchangeably with the word tumor. Neoplasm means new growth. The neoplasm can be **benign** or malignant; a cancer is a malignant neoplasm. *[Virshup, 2006, 333–334]*

A cancer is a malignant neoplasm.

To understand the difference between a benign and a malignant neoplasm, some concepts about cell growth are important to understand. The term differentiation refers to the maturation of a

cells—its structural development and specialization. Some cells do not differentiate well, and some differentiated cells revert to a lower level of differentiation. The poorly differentiated (**anaplastic**) cell does not function normally, and the more poorly differentiated cells generally divide faster. Cells in benign tumors are almost always well differentiated; cells in malignant tumors always have some loss of differentiation. Figure 8 provides an example; it shows poorly differentiated cancerous cells growing on the inner surface of the pancreas next to normal (endothelial) cells. *[Kumar, 2005, 272–273, 276]*

A well-differentiated cell has a normal, mature structure, while a poorly differentiated cell has stopped maturing at an early state or has reverted to a lower level of differentiation.

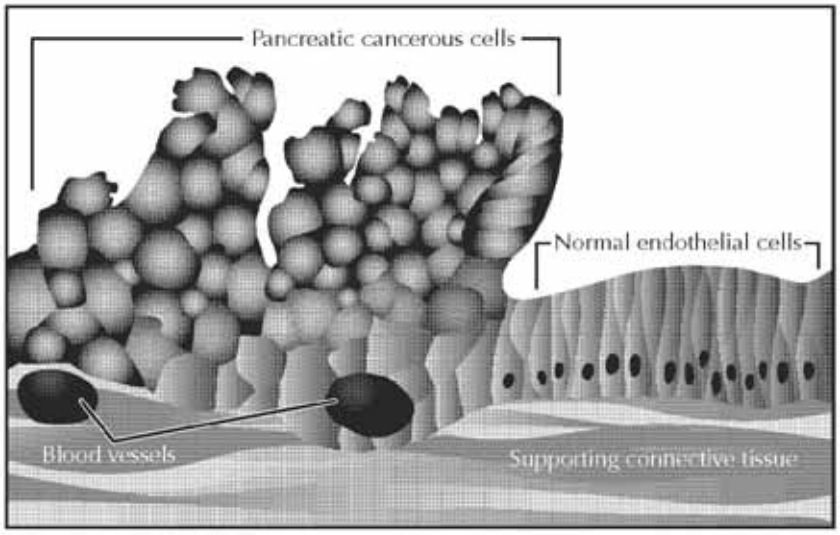


FIGURE 8

Cancerous cells: poorly differentiated cancerous cells, situated next to normal cells, are beginning to invade deeper connective tissues.

Besides growing more slowly than malignant tumors, benign tumors may be encapsulated, and they rarely spread beyond the capsule. Malignant cancers are not well encapsulated and they infiltrate, invade, and destroy surrounding tissue. In addition, their growth lacks the uniformity of normal cells. *[Kumar, 2005, 275, 278]*

Malignant tumors grow more quickly than benign tumors and are less differentiated.

Benign tumors never metastasize, that is, spread to other parts of the body. Almost all cancers have the ability to be carried to other

Malignant tumors can metastasize.

There are four major routes of cancer metastasis: blood vessels, lymphatic system, seeding of body cavities and surfaces, and transplantation.

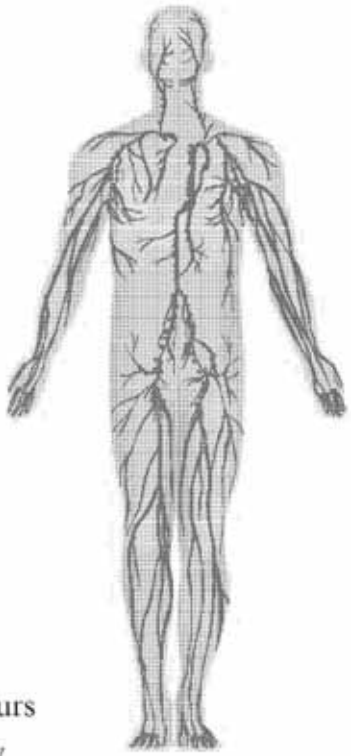
tissues of the body, implant, and begin growing there; the implant is called a metastasis. Cancers metastasize by four routes: *[Kumar, 2005, 279]*

- spread by lymphatic system
- spread by blood vessels
- seeding of body cavities and surfaces
- transplantation

Breast cancer frequently spreads by lymphatic system.

The lymphatic system carries fluids from the tissues into the blood. Lymph fluids drain through special channels and are filtered by lymph nodes. Breast cancer cells often spread first to the axillary (underarm) lymph nodes. *[Guyton, 2006, 190–192; Kumar, 2005, 279–280]*

The lymphatic system



Spread by blood vessels occurs more commonly by veins than by artery.

Spread of cancer by blood vessels occurs more commonly through veins than through arteries. This is a frequent means of cancer metastasis to the liver and lungs, because both organs have a large venous supply. Kidney cancer cells often spread after invading the renal vein. *[Kumar, 2005, 280–281]*

Cancer also spreads into open body cavities.

Spread by seeding of body cavities occurs when a cancer penetrates an open body cavity, such as the abdominal space. Ovarian cancer cells often spread in this way. *[Kumar, 2005, 279]*

Finally, transplantation spread occurs by mechanical means, such as a surgical instrument. Fortunately, this type of metastasis is rare. *[Kumar, 2005, 279]*

Transplantation spread is rare.

B. Sources of Cancer Pain

Pain may be the first symptom of cancer, as some cancers originate and develop in pain-sensitive organs such as the pancreas. As cancer advances, the incidence of pain increases. In addition, sources of pain other than the cancer itself may develop, such as pain caused by radiation and/or chemotherapy treatment. Pain in cancer patients may be: *[Willis, 2007, 196; Woodruff, 2004, 54, 62; Carver, 2005, 7, Huether, 2006, 459]*

Pain may be the first symptom of cancer.

Pain in cancer patients has four major sources.

- due to cancer itself (including pain from invasion of tissues, obstruction syndromes, nerve compression/infiltration, ulceration, and bone metastases).
- related to cancer or to debilitation resulting from cancer.
- caused by cancer treatments or diagnostic procedures.
- caused by other medical conditions.

Examples of pain caused by these sources are shown in Table 3 on the next page. Many patients experience pain from more than one source.

This section will provide further information about several common cancer pain syndromes related to the first three of these sources. The last source, other medical conditions, is a heterogeneous group of other diseases (eg, arthritis, heart disease, and diabetes mellitus) that may exist alone or in conjunction with cancer.

TABLE 3

Sources of pain in cancer patients: many patients experience pain from more than one source. Several sources of pain are due to the cancer itself.

Cause of Pain	Type of Pain
Pain due to cancer	Pain due to local invasion of tissues
	Obstruction syndromes
	Nerve compression/infiltration
	Ulceration
	Bone metastases
Pain related to cancer or disability	Bed sores
	Muscle spasms
	Constipation
	Lymphedema
	Postherpetic neuralgia
	Pulmonary embolism
	Infections
Pain due to cancer treatment	Postoperative pain
	Stump pain, phantom limb pain
	Constipation (opioid-induced)
	Postradiation inflammation/fibrosis
	Mucositis, stomatitis
	Vinca alkaloid neurotoxicity
	Bone necrosis
Pain due to other conditions	Arthritis
	Headache
	Coexisting heart disease
	Coexisting diabetes mellitus
	(Many other coexisting conditions)

Cancer may cause pain by invasion of tissues.

1. Sources Due to Cancer Itself. Cancer typically is invasive; it spreads into adjacent tissues. This can cause pain by stretching or expanding receptors in or around the tissues. Invasion can cause inflammation or swelling, stretching pain-sensitive capsules surrounding organs. *[McCance, 2006, 375, 385–386]*

Cancer itself causes pain through nociceptive and neuropathic mechanisms.

This pain has sources that are either nociceptive (somatic and visceral) or neuropathic. Somatic and visceral syndromes include bone metastases and abdominal pain syndromes, while

neuropathic syndromes include epidural metastases, peripheral neuropathies, and plexopathies. Primary or metastatic cancer may invade or compress peripheral nerves (peripheral neuropathies) or the spinal cord (e.g., epidural metastases). This can result in neuropathic pain and numbness. *[Woodruff, 2004, 62; Carver, 2005, 7; de Leon-Casasola, 2008, S3]*

a. Bone metastases. Destruction of bone by metastatic tumors is the most common cause of pain in patients with cancer. Bone pain may be the first symptom in a patient with cancer originating in the bone or bone marrow, or bone pain may signal the spread of the disease. *[McCance, 2006, 386; Shaiova, 2006, 334; Carver, 2005, 7]*

Destruction of bone by metastatic tumors is the most common cause of cancer pain.

Cancer often metastasizes to bone from cancerous sites in the breast, prostate, thyroid, and lung. The most common sites of bone metastasis are the vertebrae. The pain is usually a result of direct tumor invasion and can be severe. Multiple sites of bone invasion and pain are common; the pain is typically dull and throbbing and is made worse by movement. The pain may be referred (eg, hip pain may refer to the knee or the groin). Bone invasion pain is typically responsive to opioid therapy. *[McCance, 2006, 386; Shaiova, 2006, 332, 334–335; Woodruff, 2004, 62]*

The most common sites of bone metastasis are the vertebrae.

Bone tumors in the vertebrae may also impinge upon nerve roots and result in **radicular** pain, or they can spread into the epidural space and produce severe and rapidly progressive pain. Involvement of the upper spine may result in head and neck pain. Thus, in addition to causing somatic pain, vertebral metastases (tumors) may also cause neuropathic pain. Bone metastases may lead to additional complications, such as bone fractures and spinal cord compression. If untreated, spinal cord compression can lead to paralysis. *[Carver, 2005, 7; Shaiova, 2006, 334; Boss, 2006, 583]*

In addition to causing somatic pain, vertebral tumors may cause neuropathic pain.

Abdominal tumors cause visceral pain through a variety of mechanisms.

b. Abdominal pain syndromes. Abdominal tumors frequently cause visceral pain through a variety of mechanisms: *[Shaiova, 2006, 337]*

- infiltration of tumors
- obstruction, distention, or stretching of viscera
- inflammation of membrane

Visceral pain caused by tumors can be intermittent or continuous, and may be referred to other parts of the body.

Visceral pain caused by tumors can be intermittent or continuous and may be accompanied by other symptoms, such as fatigue, nausea, and sweating. Pain may be referred to the skin above or near the affected site. For example, pancreatic and endometrial tumors may be felt as back pain, and liver tumors may be felt as shoulder pain. *[Shiaova, 2006, 337–378]*

A tumor may obstruct the structure it is growing in or a nearby structure.

Visceral pain is most common when malignant tumors cause distention. The tumor may also cause obstruction in the structure in which it is growing or by pressing against a nearby structure. For example, prostate cancer can result in renal obstruction; gastrointestinal cancers and ovarian cancer can result in intestinal obstruction. Intestinal obstruction causes a **colicky** pain along with nausea, vomiting, and bloating. Opioid therapy may be used to manage some types of visceral pain. Surgery may be required to relieve some obstructions, such as intestinal blockage (see Figure 9). *[Shiaova, 2006, 337–378; Chang, 2006, 1424]*

c. Peripheral neuropathies. Individual peripheral nerves can be compressed, injured, or infiltrated by tumor, causing neuropathy. As a result, the peripheral neurons may produce an increased or exaggerated signal in response to mildly painful stimuli (hyperalgesia) or may signal in response to nonpainful stimuli, resulting in the perception of pain from stimuli (eg, a light touch) not associated with pain allodynia). Additionally, abnormal nerve regrowth may occur after injury, resulting in non-pain fibers regrowing in

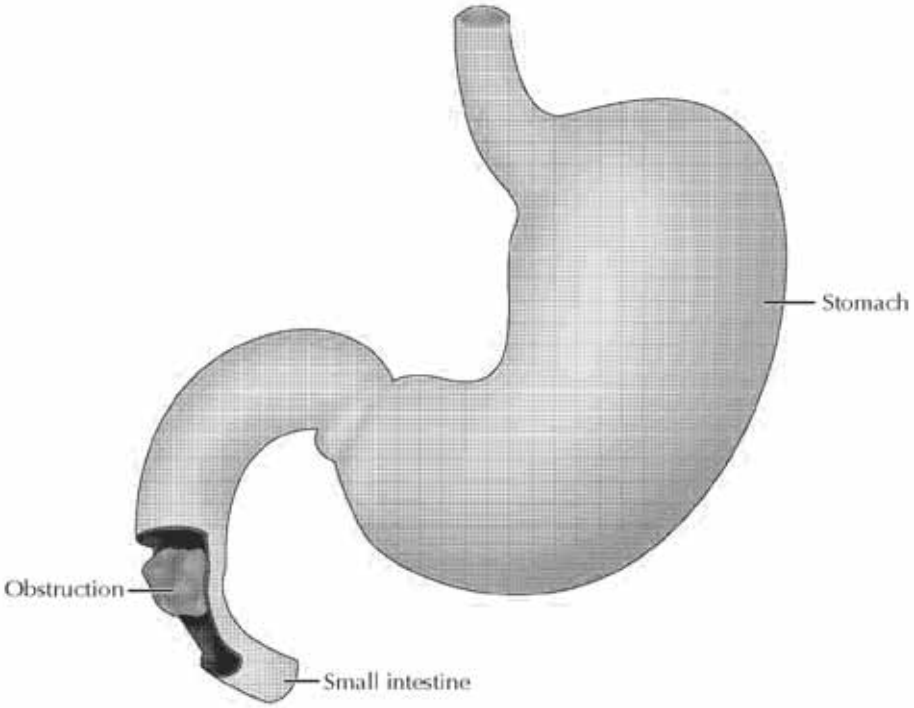


FIGURE 9

Intestinal obstruction: cancer can cause painful obstructions of the viscera and other organ systems.

regions that normally contain C fibers. This also results in pain perception to nonpainful stimuli. Peripheral neuropathies are characterized by pain that ranges from tingling to excruciating pain. Motor and sensory impairment may also occur. Opioids may help to decrease the severity of neuropathic pain. *[Chang, 2006, 1423; Boss, 2006, 594]*

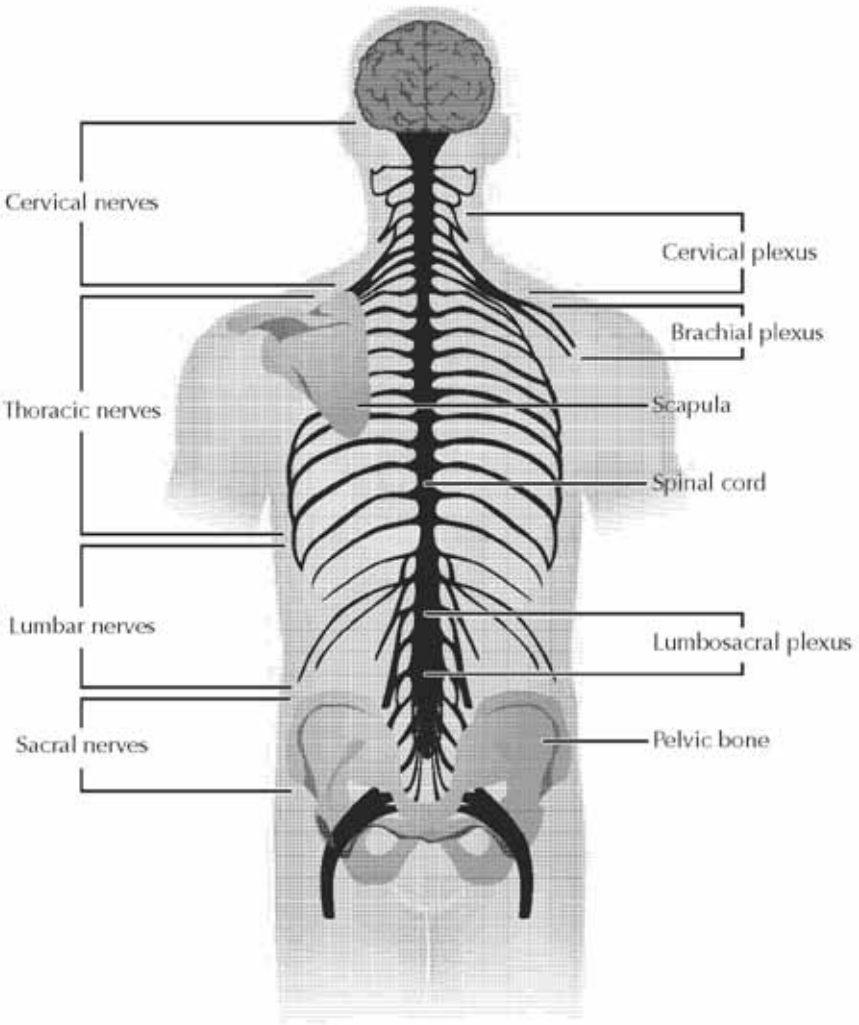
Peripheral neuropathies can be characterized by sensory and motor impairment, and pain ranging from mild to severe.

d. Plexopathies. Some peripheral nerves link together in a network or bundle of nerves known as a **plexus**. Head and neck cancers may infiltrate the cervical plexus (in the neck); lung, breast, or thyroid cancers may infiltrate the brachial plexus (in armpit region); and colon or cervical cancers may infiltrate the lumbar plexus (in abdominal area). These are examples of plexopathies (see Figure 10 on the next page). *[Sugerman, 2006, 432; Lussier, 2004, 579]*

Some peripheral nerves link together in a network of nerves known as a plexus.

FIGURE 10

Peripheral nerves and selected nerve plexuses: the cervical, brachial, and lumbosacral plexuses are complex networks of nerves carrying sensory and motor information to and from specific body areas.



Pain occurs when plexuses are infiltrated by tumor or affected by treatment.

Just as radicular pain may occur if a spinal nerve is compressed, pain may also occur when these plexuses are infiltrated by tumor or affected by radiation treatment. *[Lussier, 2004, 579]*

2. Sources Related to Cancer or Cancer Debilitation. Cancer and its treatments may debilitate the patient, increasing the vulnerability to diseases or **opportunistic infections** that can also cause significant pain. *[Woodruff, 2004, 62; McCance, 2006, 386]*

a. Myofascial pain. Patients with advanced cancer are especially prone to myofascial pain. Muscle spasm, tenderness, and stiffness cause pain that can be mild to severe. Myofascial pain can become chronic and disabling. *[Woodruff, 2004, 62; Huether, 2006, 458]*

Patients with advanced cancer are prone to myofascial pain, which can become disabling.

b. Acute and postherpetic neuralgia. Chemotherapy and related cancer treatments can suppress the immune system and create opportunities for infections. Herpes zoster virus remains dormant in the nervous system indefinitely after the varicella symptoms have disappeared. In immunosuppressed patients, the virus may become active again and attack peripheral nerves. A rash develops, typically at the site most affected by the initial infection. The accompanying pain may be severe. Postherpetic neuralgia is a common, difficult to treat complication of herpes zoster, lasting 1 to 6 months. *[Woodruff, 2004, 63; Mattiuzzi; 2008, 976; Alakloby, 2008, 457–458]*

Chemotherapy and other cancer treatments can suppress the immune system.

Herpes zoster virus may become reactivated in immunosuppressed patients. Postherpetic neuralgia can be severe and difficult to treat.

Other painful effects of debilitating disease include pressure sores, gastric distention, bladder spasms, and **thrombosis.** *[Woodruff, 2004, 63]*

3. Sources Due to Cancer Treatments. About 20% of cancer pain is thought to be due to treatments. Surgery, chemotherapy, radiation, and other treatments can have harmful effects on somatic and nerve tissues. *[Chang, 2006, 1415; Lussier, 2004, 570]*

About 20% of all cancer pain is thought to be due to cancer treatments.

a. Mucositis. Almost all cancer patients receiving radiation therapy for head and neck cancers develop mucositis, inflammation of the mucus membranes inside the mouth. The inflammation causes severe and long-lasting symptoms, including difficulty swallowing, excess mucus, and weight loss, in addition to pain. *[Rosenthal, 2008, 1]*

Mucositis can cause severe and long-lasting symptoms.

b. Plexopathies. In addition to tumor-related causes, pain occurs when plexuses are compressed by **fibrosis** after radiation therapy to adjacent areas. *[Lussier, 2004, 579]*

When nerve plexuses are compressed by radiation-induced fibrosis, pain occurs.

A variety of cancer treatments can cause peripheral neuropathies.

c. Peripheral neuropathies. In addition to compression/infiltration by tumor, diagnostic procedures and treatments, such as surgery, chemotherapy, and radiation therapy can also cause neuropathy. *[Woodruff, 2004, 63; Lussier, 2004, 579]*

C. Patterns and Characteristics of Breakthrough Cancer Pain

Section II introduced three basic cancer pain patterns: intermittent (episodic), persistent, and breakthrough. Intermittent pain typically occurs early in the course of cancer. As pain progresses, patients typically develop persistent pain accompanied by breakthrough pain. Recall that breakthrough pain is a transitory flare of moderate to severe pain over a baseline of otherwise controlled persistent pain.

Breakthrough pain is a transitory flare of moderate to severe pain over a baseline of otherwise controlled persistent pain.

Studies indicate that 51%–89% of cancer-pain patients report episodes of breakthrough pain.

In a large, prospective survey of cancer pain patients experiencing moderate to severe chronic pain, 51%–89% of patients reported episodes of breakthrough pain. Overall, breakthrough pain is common in patients with chronic pain. The three types of breakthrough pain, which were introduced in Section II, are the following. *[Payne, 2007, S4]*

Incident pain occurs when a specific event causes the pain.

- Incident pain is pain in which a precipitating event can be identified (eg, standing, walking, and coughing). This is the most common type of breakthrough pain, accounting for about 50% of breakthrough pain episodes,

Breakthrough pain with no identifiable precipitating event is called spontaneous/idiopathic.

- Spontaneous/idiopathic pain is pain that occurs with no identifiable precipitating cause.

End-of-dose failure pain occurs at the end of the ATC dosing cycle.

- End-of-dose failure pain occurs at the end of the dosing interval for medication given by around-the-clock (ATC) dosing; some argue that this is not appropriately classed as a form of breakthrough pain. It is usually managed by adjusting the ATC medication.

The pathophysiology of breakthrough pain may be somatic, visceral, or neuropathic. The source is typically the same as the persistent pain.

The pathophysiology of breakthrough pain may be somatic, visceral, or neuropathic.

Breakthrough pain can be described by its temporal characteristics, such as onset, duration, and frequency. The onset of breakthrough pain can escalate to a maximum intensity in as little as 3 minutes. The majority of episodes last 120 minutes or less. *[Payne, 2007, S5; Portenoy, 2006, 586]*

Episodes of breakthrough pain may reach peak intensity within 3 minutes and usually last 120 minutes or less.

The number of episodes of breakthrough pain occurring each day is typically 4–7 episodes. This number can be modified to some degree depending on how aggressively the ATC medication is titrated. *[Portenoy, 2006, 586; McCarberg, 2007, S9]*

Breakthrough pain is typically experienced 4–7 times per day.

Summary

Cancerous tumors frequently cause pain, which can be due to the cancer itself, related to cancer/ cancer debilitation, caused by treatments, or caused by other, unrelated conditions.

- Abdominal syndromes have pain arising from two mechanisms: obstructive blockages and non-obstructive sources (eg, pancreatic or liver distention).
- Bone metastases are most common in the vertebrae, but tumors commonly invade multiple bone sites, causing severe pain.
- Invasion or compression of peripheral nerves by tumors results in sensory loss, weakness, and abnormal sensations in the areas innervated by the nerve.
- Plexopathies result from tumor infiltration of peripheral nerve plexuses, with resulting abnormal, painful sensations.
- Cancer treatments can induce severe oral/throat inflammation (mucositis) and can also cause plexopathies and peripheral neuropathies.
- In a survey of cancer patients, 51%–89% reported episodes of breakthrough pain.
- There are three types of breakthrough pain: incident, spontaneous/idiopathic, and end-of-dose failure. Breakthrough pain can escalate to maximum intensity within 3 minutes and usually lasts 120 minutes or less. Episodes usually occur 4–7 times per day.

Review Questions (V)

DIRECTIONS. Circle the letter corresponding to the correct response in each of the following items.

1. An estimated _____ of advanced cancer patients report significant pain.

   a. one quarter
   b. one third
   c. two thirds
   d. three quarters

2. Which of the following is **not** a means of cancer metastasis?

   a. by blood flow
   b. by metabolites
   c. by seeding of body cavities
   d. through the lymphatic system

3. Nociceptive abdominal pain is frequently

   a. colicky.
   b. epidural.
   c. lancinating.
   d. radicular.

4. Tumor compression of a nerve root results in _____ pain.

   a. colicky
   b. epidural
   c. lancinating
   d. radicular

5. Peripheral neuropathies are caused by

   a. chemotherapy.
   b. fibrosis compression.
   c. tumor infiltration.
   d. all of the above

6. Mucositis is a(n)

   a. adverse effect of chemotherapy and of head/neck radiation.

   b. adverse effect of incisions during head/neck surgery.

   c. form of oral cancer.

   d. result of tumor invasion of a cranial nerve.

7. In patients already experiencing moderate to severe chronic cancer pain, studies on breakthrough pain have reported a prevalence of _____.

   a. 12%–19%
   b. 24%–36%
   c. 51%–89%
   d. 77%–92%

8. Which of the following is/are characteristic of breakthrough pain?

   a. occurrence 4–7 times per day
   b. rapid onset
   c. relatively short duration
   d. all of the above

9. The most common source of pain in cancer patients is

   a. bone metastases.
   b. direct tissue invasion.
   c. nerve compression.
   d. obstruction.

Check your responses on page 69.

Integrative Summary

- Nociceptors throughout the body carry pain signals in A-delta and C fibers to neurons in the spinal cord. The transmitters of pain at these neural junctures are glutamate and substance P.
- Strong tactile stimulation carried into the spinal cord by A-beta fibers can block pain transmission by overloading the transmission pathways.
- Descending pathways from the brain lead to inhibitory interneurons in the spinal cord that use natural opiates (endorphins) to stop the release of substance P and block pain.
- Pain can either be acute or chronic in duration and is classified as mild, moderate, or severe.
- While persistent pain is always present, breakthrough pain appears against a background of otherwise controlled persistent pain.
- Breakthrough pain is a transitory exacerbation or flare of moderate to severe pain in patients with otherwise stable persistent pain who are taking chronic opioid therapy. It is common in patients with chronic pain.
- A number of pain assessment scales are available.
- Good rapport between the physician and patient can help assure that the assessment is accurate.
- Pharmacologic treatments for persistent pain should use around-the-clock (ATC) dosing, not as-needed (PRN) dosing. The desirable dose for any given patient is the dosage providing optimal pain relief with tolerable adverse effects.

- ATC medications are used to prevent persistent pain, while supplemental medications are used to relieve breakthrough pain.
- Pain is frequently undertreated for reasons ranging from inadequate professional education, to denial/underreporting of pain by patients, to lack of insurance coverage for pain treatment procedures.
- Tolerance, physical dependence, and addiction are often of concern to patients and professionals. Under medical supervision, appropriate use of opioids rarely leads to addiction.
- There are multiple sources of cancer pain, including pain due to the cancer itself, pain related to cancer debilitation, pain caused by cancer treatments, and pain related to other medical conditions.
- It is estimated that 30% to 40% of patients have moderate-to-severe pain at the time of diagnosis and at intermediate stages. For patients receiving active anticancer treatment, 40%–70% have this level of pain.
- Pain may be due to the cancer itself, to debilitation from cancer, or from cancer treatments.

Answers to Review Questions

I. 1. c (page 14, paragraph 1)
2. a (page 16, paragraph 2)
3. a (page 18, paragraph 4)
4. a (page 19, paragraph 4)
5. a (page 20, paragraph 2)

II. 1. c (page 25, paragraph 3)
2. c (page 26, paragraph 3; page 30, paragraph 1)
3. a (page 27, paragraph 1)
4. d (page 30, paragraph 4; page 31, paragraph 1)

III. 1. d (page 35, paragraphs 2–4)
2. c (page 35, paragraph 5)
3. a (page 36, paragraph 3)
4. d (page 37, paragraph 2)
5. d (page 39, paragraphs 2 and 3)

IV. 1. d (page 44, paragraph 3; page 45, paragraphs 3 and 4)
2. c (page 47, paragraph 2)
3. d (page 48, paragraph 1)

V. 1. c (page 52, paragraph 1)
2. b (page 53, paragraph 1)
3. a (page 58, paragraph 3)
4. d (page 57, paragraph 4)
5. d (page 62, paragraph 1)
6. a (page 61, paragraph 5)
7. c (page 62, paragraph 3)
8. d (page 63, paragraphs 2 and 3)
9. a (page 57, paragraph 2)

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